

Dependent claims 66, 72-77

65: Independent method of suppressing autoimmune
disease claim (p. 44)

Dependent claims 67, 78-82

NEW CLAIMS:

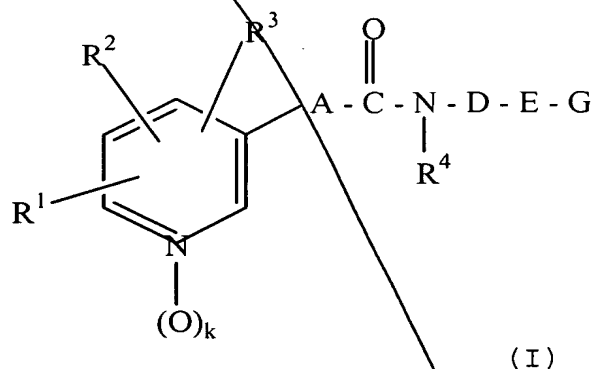
68: composition (p. 52)

69: method of producing (p. 56)

70: composition (p. 63)

71: composition (p. 66)

42. (once amended) A compound of formula (I) and pharmaceutically acceptable salts of formula (I)



wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_4 -hydroxyalkyl, hydroxy, C_1 - C_4 -alkoxy, benzyloxy, C_2 - C_4 -alkanoyloxy, C_1 - C_4 -alkylthio, C_2 - C_5 -alkoxycarbonyl, aminocarbonyl, C_3 - C_9 -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6 , and bridged R^1R^2 wherein

R^5 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl; and

R^6 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, C_1 - C_6 -alkyl, trifluoromethyl and hydroxy and bridged R^1R^2 ;

wherein

D'
Cont
C'
~~bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein~~

~~R^7 is selected from the group consisting of hydrogen, and C_1-C_6 -alkyl; and~~

~~R^8 is selected from the group consisting of hydrogen and C_1-C_6 -alkyl;~~

~~R^3 is selected from the group consisting of hydrogen, halogen and C_1-C_6 -alkyl;~~

~~R^4 is selected from the group consisting of hydrogen, C_1-C_6 -alkyl, C_3-C_6 -alkenyl, hydroxy, C_1-C_6 -alkoxy and benzyloxy;~~

~~k is 0 or 1,~~

~~A is selected from the group consisting of C_2-C_6 -alkenylene, .~~

~~a substituted C_2-C_6 -alkenylene which is substituted one to three-fold by C_1-C_3 -alkyl, hydroxy, fluorine, cyano, or phenyl, C_4-C_6 -alkadienylene,~~

~~a substituted C_4-C_6 -alkadienylene which is substituted once or twice by C_1-C_3 -alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,~~

~~a substituted 1,3,5-hexatrienylene which is substituted by C_1-C_3 -alkyl, fluorine, or cyano, and ethynylene;~~

~~D is selected from the group consisting of C_1-C_{10} -alkylene,~~

~~a substituted C_1-C_{10} -alkylene which is substituted once or twice by C_1-C_3 -alkyl or hydroxy,~~

~~C_2-C_{10} -alkenylene,~~

a substituted C_2 - C_{10} -alkenylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy,

a substituted C_2 - C_{10} -alkenylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy, wherein the double bond is to E,

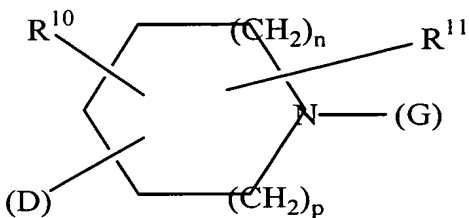
C_3 - C_{10} -alkynylene,

a substituted C_3 - C_{10} -alkynylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy,

an isosterically replaced C_1 to C_{10} group selected from the group consisting of C_1 - C_{10} -alkylene, C_2 - C_{10} -alkenylene and C_3 - C_{10} -alkynylene, the isosterically replaced C_1 to C_{10} group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR^9 , CO, SO or SO_2 ; wherein

R^9 is selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, C_2 - C_6 -acyl and methanesulfonyl;

E is



wherein n and p are, independent of each other, 0, 1, 2, or 3, wherein $n + p \leq 3$,

R^{10} is selected from the group consisting of hydrogen, C_1 -

C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;

D1
cont

C1

 R^{11} is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, G1, G2, G3, G4 and G5; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$
wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of hydrogen,

C₁-C₆-alkyl,

C₃-C₆-alkenyl,

C₃-C₆-alkinyl,

C₃-C₈-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, which heterocycles are either bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an

aromatic or a hydrogenated ring and either directly or over a methylene group, and

D' cont
C1
a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group;

R¹³ has the same meaning as R¹², but is selected independently thereof,

R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl,

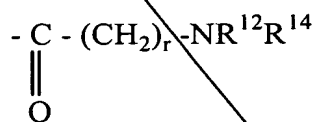
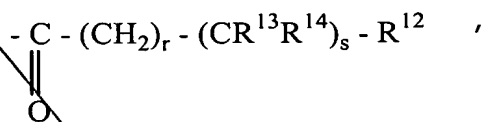
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

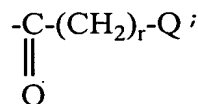
a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with

a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

G2 is selected from the group consisting of



and



wherein R^{12} and R^{14} have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

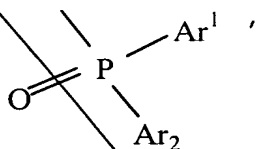
saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, and

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside

from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$,

G4 is



wherein

Ar^1 is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar^2 is selected from the group consisting of phenyl, pyridyl and naphthyl;

G5 is $-\text{COR}^{15}$,

wherein

R^{15} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy and benzyloxy; and

wherein aromatic rings in R^1 , R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q, Ar^1 and Ar^2 are unsubstituted or substituted, the substituted rings in R^1 , R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q, Ar^1 and Ar^2 having one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, phenyl, benzyl, hydroxy, C_1 - C_6 -alkoxy, and a

B1
cont
C1

substituted C₁-C₆-alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆ alkoxy may form an additional ring over a methylenedioxy bridge, wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide.

43. (once amended) A compound according to claim 42, wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, methyl, trifluoromethyl, hydroxy, C₁-C₄-alkoxy, ethylthio, methoxycarbonyl, tert-butoxycarbonyl, aminocarbonyl, carboxy, and phenoxy,

R² is selected from the group consisting of hydrogen, halogen, trifluoromethyl and hydroxy,

R³ is hydrogen or halogen,

R⁴ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy and C₁-C₃-alkoxy,

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once or twice by C₁-C₃-alkyl, hydroxy or fluorine,

81
cont

a C₄-C₆-alkadienylene,
a substituted C₄-C₆-alkadienylene which is substituted
by C₁-C₃-alkyl or by 1 or 2 fluorine atoms,
1,3,5-hexatrienylene, and
a substituted 1,3,5-hexatrienylene which is substituted
by fluorine,

C1

D is selected from the group consisting of C₁-C₈-alkylene,

a substituted C₁-C₈-alkylene which is substituted once or twice by methyl or hydroxy,

C₂-C₈-alkenylene,

a substituted C₂-C₈-alkenylene which is substituted once or twice by methyl or hydroxy,

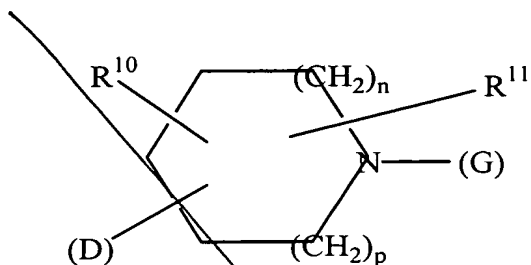
an E double bonded substituted C₂-C₈-alkenylene which has a double bond to ring E,

C₃-C₈-alkynylene,

a substituted C₃-C₈-alkynylene which is substituted once or twice by methyl or hydroxy, and

an isosterically replaced C1 to C8 group selected from the group consisting of C₁-C₈-alkylene, C₂-C₈-alkenylene and C₃-C₈-alkynylene, the isosterically replaced C1 to C8 group having methylene units and one to three methylene units are isosterically replaced by O, S, NH, N(CH₃), N(COCH₃), N(SO₂CH₃), CO, SO or SO₂,

E is



C1

wherein n and p are, independent of each other, 0, 1, 2, or 3, wherein $n + p \leq 3$,

R^{10} is selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, hydroxy, hydroxymethyl, carboxy and C_2 - C_7 -alkoxycarbonyl;

R^{11} is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, G1, G2, G3, G4 and G5; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_8 -cycloalkyl, benzyl, phenyl, benzocyclobutyl, indanyl, indenyl, oxoindanyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, oxotetrahydronaphthyl, biphenylenyl, fluorenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, phenanthryl, dihydrophenanthryl, oxodihydrophenanthryl,

D'
ant

Cl

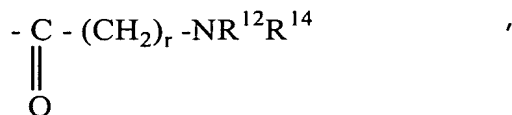
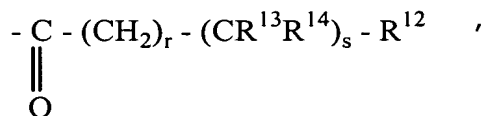
dibenzocycloheptenyl, oxodibenzocycloheptenyl,
dihydrodibenzocycloheptenyl, oxodihydrodibenzocycloheptenyl,
dihydrodibenzocyclooctenyl, tetrahydrodibenzocyclooctenyl and
oxotetrahydrodibenzocyclooctenyl, bound directly or over a
methylene group, furyl, thienyl, pyrrolyl, oxazolyl,
isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl,
oxadiazolyl, thiadiazolyl, triazolyl, pyridyl, pyrazinyl,
pyridazinyl, pyrimidinyl, triazinyl, imidazothiazolyl,
benzofuryl, dihydrobenzofuryl, benzothienyl,
dihydrobenzothienyl, indolyl, indolinyl, oxoindolinyl,
dioxoindolinyl, benzoxazolyl, oxobenzoxazolyl,
benzisoxazolyl, oxobenzisoxazolyl, benzothiazolyl,
oxobenzthiazolyl, benzoisothiazolyl, oxobenzoisothiazolyl,
benzimidazolyl, oxobenzimidazolyl, indazolyl,
oxoindazolyl, benzofurazanyl, benzothiadiaazolyl,
benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl,
thiazolopyridyl, oxodihydrothiazolopyridyl,
isothiazolopyridyl, imidazopyridyl, oxodihydroimidazopyridyl,
pyrazolopyridyl, oxodihydropyrazolopyridyl, thienopyrimidinyl,
chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl,
isoquinolyl, dihydroquinolyl, oxodihydroquinolyl,
tetrahydroquinolyl, oxotetrahydroquinolyl, benzodioxanyl,
quinoxalyl, quinazolyl, naphthyridinyl, carbazolyl,
tetrahydrocarbazolyl, oxotetrahydrocarbazolyl, pyridoindolyl,
acridinyl, oxodihydroacridinyl, phenothiazinyl,
dihydrodibenzoxepinyl, oxodihydrodibenzoxepinyl,
benzocycloheptathienyl, oxobenzocycloheptathienyl,
dihydrothienobenzothiepinyl, oxodihydrothienobenzothiepinyl,
dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl,
octahydrodibenzothiepinyl, dihydrodibenzazepinyl,
oxodihydrodibenzazepinyl, octahydrodibenzazepinyl,
benzocycloheptapyridyl, oxobenzocycloheptapyridyl,

9' cont
dihydropyridobenzodiazepinyl, dihydrodibenzoxazepinyl, dihydropyridobenzoxepinyl, dihydropyridobenzoxazepinyl, oxodihydropyridobenzoxazepinyl, dihydrodibenzothiazepinyl, oxodihydrodibenzothiazepinyl, dihydropyridobenzothiazepinyl, and oxodihydropyridobenzothiazepinyl, bound directly or over a methylene group,

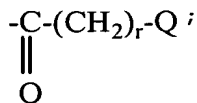
C1
R¹³ has the same meaning as R¹², but is selected independently therefrom,

R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl, indanyl, indenyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, triazinyl, benzofuryl, benzothienyl, indolyl, indolinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl, and tetrahydroquinolyl, bound directly or over a methylene group,

G2 is selected from the group consisting of



and



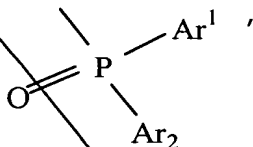
C'

wherein R^{12} and R^{14} have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of azetidene, pyrrolidine, piperidine, (1H)tetrahydropyridine, hexahydroazepine, (1H)tetrahydroazepine, octahydroazocine, pyrazolidine, piperazine, hexahydrodiazepine, morpholine, hexahydrooxazepine, thiomorpholine, thiomorpholine-1,1-dioxide, 5-aza-bicyclo[2.1.1]hexane, 2-aza-bicyclo[2.2.1]heptane, 7-aza-bicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, 2-aza-bicyclo[2.2.2]octane, 8-aza-bicyclo[3.2.1]octane, 2,5-diazabicyclo[2.2.2]octane, 9-azabicyclo[3.3.1]nonane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydroquinoxaline, (4H)-dihydrobenzoxazine, (4H)-dihydrobenzothiazine, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[c]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole, (10H)-dihydroacridine, 1,2,3,4-tetrahydroacridanone, (10H)-phenoxazine, (10H)-phenothiazine, (5H)-dibenzazepine, (5H)-dihydrodibenzazepine, (5H)-octahydrodibenzazepine, (5H)-dihydrodibenzodiazepine, (11H)-dihydrodibenzo[b,e]oxazepine, (11H)-dihydrodibenzo[b,e]thiazepine, (10H)-dihydrodibenzo[b,f]oxazepine, (10H)-

dihydrodibenzo[b,f]thiazepine, and
(5H)-tetrahydrodibenzazocine,

G3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$,

G4 is



wherein

Ar^1 and

Ar^2 are selected independently of each other from the group consisting of phenyl, pyridyl and naphthyl;

G5 is $-\text{COR}^{15}$,

wherein

R^{15} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy and benzyloxy; and

wherein aromatic rings are substituted or unsubstituted independently of each other by one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, phenyl, benzyl, hydroxy, C_1 - C_6 -alkoxy, and a substituted C_1 - C_6 -alkoxy which is entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C_1 - C_6 -alkylthio, carboxy, C_1 - C_6 -alkoxycarbonyl,

benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C1-C6 alkoxy may form an additional ring over a methylenedioxy bridge.

D1
cont 44. (once amended) A compound according to claim 43 wherein:

C1 R¹ is selected from the group consisting of hydrogen, halogen, cyano, methyl, trifluoromethyl, hydroxy, methoxy and methoxycarbonyl,

R² is hydrogen or halogen,

R³ is hydrogen,

R⁴ is selected from the group consisting of hydrogen, C₁-C₃-alkyl and hydroxy,

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once or twice by hydroxy or fluorine,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted by one or two fluorine atoms, and

1,3,5-hexatrienylene

D is selected from the group consisting of C₂-C₈-alkylene, a substituted C₂-C₈-alkylene which is substituted by

methyl or hydroxy

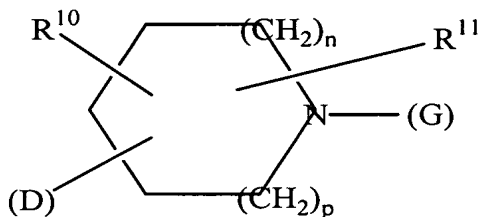
C₂-C₈-alkenylene,

a substituted C₂-C₈-alkenylene which is substituted by methyl or hydroxy,

a substituted C₂-C₈-alkenylene which is substituted by methyl or hydroxy, wherein the double bond is to ring E,

an isosterically replaced C₂ to C₈ group selected from the group consisting of C₂-C₈-alkylene and C₂-C₈-alkenylene, the isosterically replaced C₂ to C₈ group having methylene units and one to three of the methylene units are isosterically replaced by O, NH, N(CH₃), N(COCH₃), N(SO₂CH₃) or CO,

E is



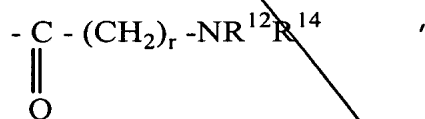
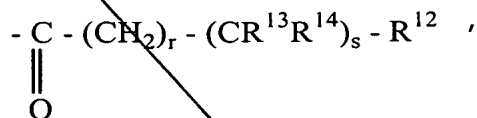
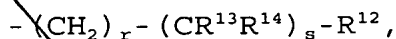
wherein **n** and **p** are, independent of each other, 0, 1, 2, or 3, wherein $n + p \leq 3$,

R¹⁰ is selected from the group consisting of hydrogen, methyl and hydroxyl,

R¹¹ is hydrogen or an oxo group adjacent to the nitrogen atom,

G is selected from the group consisting of hydrogen, C₃-

C₈-cycloalkyl, methoxycarbonyl, tert-butoxycarbonyl,
benzyloxycarbonyl, trifluoroacetyl, diphenylphosphinoyl,



and



wherein

r is 0, 1 or 2,

s is 0 or 1,

R¹² is selected from the group consisting of hydrogen, methyl, benzyl, phenyl, indanyl, indenyl, oxoindanyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, oxotetrahydronaphthyl, flourenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, dibenzocycloheptenyl, and oxodibenzocycloheptenyl, dihydrodibenzocycloheptenyl, oxodihydrodibenzocycloheptenyl bound directly or over a methylene group, furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl,

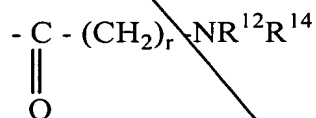
D1
Cont
C1
pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl,
imidazothiazolyl, benzofuryl, dihydrobenzofuryl, benzothienyl,
dihydrobenzothienyl, indolyl, indolinyl, oxoindolinyl,
dioxoindolinyl, benzoxazolyl, oxobenzoxazolyl,
benzisoxazolyl, oxobenzisoxazolyl, benzothiazolyl,
oxobenzthiazolyl, benzoisothiazolyl, oxobenzoisothiazolyl,
benzimidazolyl, oxobenzimidazolyl, benzofurazanyl,
benzothiadiazolyl, benzotriazolyl, oxazolopyridyl,
oxodihydrooxazolopyridyl, thiazolopyridyl,
oxodihydrothiazolopyridyl, isothiazolopyridyl, imidazopyridyl,
oxodihydroimidazopyridyl, pyrazolopyridyl, thienopyrimidinyl,
chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl,
isoquinolyl, dihydroquinolyl, oxodihydroquinolyl,
tetrahydroquinolyl, oxotetrahydroquinolyl, benzodioxanyl,
quinoxalyl, quinazolyl, naphthyridinyl, carbazolyl,
tetrahydrocarbazolyl, oxotetrahydrocarbazolyl, pyridoindolyl,
acridinyl, oxodihydroacridinyl, phenothiazinyl,
dihydrodibenzoxepinyl, benzocycloheptathienyl,
oxobenzocycloheptathienyl, dihydrothienobenzothiepinyl,
oxodihydrothienobenzothiepinyl, dihydrodibenzothiepinyl,
oxodihydrodibenzothiepinyl, dihydrodibenzazepinyl,
oxodihydrodibenzazepinyl, octahydrodibenzazepinyl,
benzocycloheptapyridyl, oxobenzocycloheptapyridyl,
dihydropyridobenzoxepinyl, dihydrodibenzothiazepinyl, and
oxodihydrodibenzothiazepinyl, bound directly or over a
methylene group,

R¹³ is selected from the group consisting of hydrogen,
methyl, benzyl and phenyl,

R¹⁴ is selected from the group consisting of hydrogen,
hydroxy, methyl, benzyl, phenyl, naphthyl, furyl, thienyl,

91
Cont
oxazolyl, thiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, pyridyl, benzofuryl, benzothienyl, indolyl, indolinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl and tetrahydroquinolyl, bound directly or over a methylene group,

wherein in formula



CI
-NR¹²R¹⁴ may be selected from the group consisting of pyrrolidine, piperidine, (1H)-tetrahydropyridine, hexahydroazepine, octahydroazocine, piperazine, hexahydrodiazepine, morpholine, hexahydrooxazepine, 2-azabicyclo[2.2.1]heptane, 7-azabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, 8-azabicyclo[3.2.1]octane, 2,5-diazabicyclo[2.2.2]octane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydroquinoxaline, (4H)-dihydrobenzoxazine, (4H)-dihydrobenzothiazine, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indol, (10H)-dihydroacridine, 1,2,3,4-tetrahydroacridanone, (5H)-dihydrodibenzazepine, (5H)-dihydrodibenzodiazepine, (11H)-dihydrodibenzo[b,e]oxazepine, (11H)-dihydrodibenzo[b,e]thiazepine, (10H)-dihydrodibenzo[b,f]oxazepine and (5H)-tetrahydrodibenzazocine,

wherein aromatic rings are substituted or unsubstituted independently of each other by one to three substituents independently selected from the group consisting of halogen,

D1
ant

cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, and a substituted C₁-C₆-alkoxy entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆ alkoxy form an additional ring over a methylenedioxy bridge.

C1

45. (once amended) A compound according to claim 22, wherein

R¹ is selected from the group consisting of hydrogen, fluorine, chlorine, bromine, methyl, trifluoromethyl and hydroxy,

R² and

R³ are hydrogen,

R⁴ is hydrogen or hydroxy,

k is 0 or 1,

A is selected from the group consisting of C₂-C₄-alkenylene,

1,3-butadienylene,

a C₂-C₄-alkenylene substituted by fluorine, and

a 1,3-butadienylene substituted by fluorine,

D is selected from the group consisting of C₂-C₆-alkylene, C₂-C₆-alkenylene,

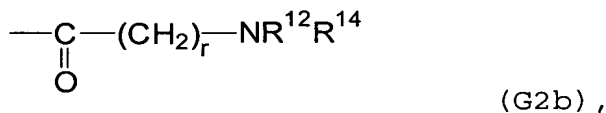
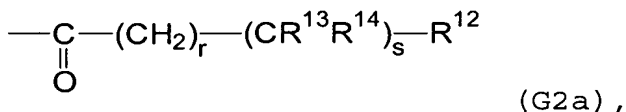
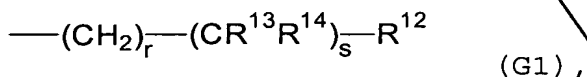
C₂-C₆-alkylene and C₂-C₆-alkenylene wherein the double

bond is to ring E, and

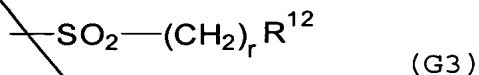
D/ Cont an isosterically replaced C2 to C6 group selected from the group consisting of C₂-C₆-alkylene and C₂-C₆-alkenylene, the isosterically replaced C2 to C6 group having a methylene unit which is isosterically replaced by O, NH, N(CH₃) or CO, or an ethylene group which is isosterically replaced by NH-CO or CO-NH, or a propylene group which is isosterically replaced by NH-CO-O or O-CO-NH,

C1 E is selected from the group consisting of piperidine, and a substituted piperidine wherein the heterocyclic ring is substituted by an oxo group adjacent to the nitrogen atom,

G is selected from the group consisting of hydrogen, tert-butoxycarbonyl, diphenylphosphinoyl,



and



19' *cont*
wherein

cl
 r is 0 or 1,

s is 0 or 1,

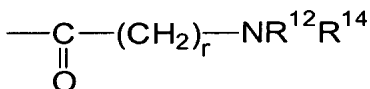
R^{12} is selected from the group consisting of hydrogen, methyl, benzyl, phenyl, indenyl, oxoindanyl, naphthyl, tetrahydronaphthyl, fluorenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, dibenzocycloheptenyl, and dihydrodibenzocycloheptenyl, bound directly or over a methylene group, furyl, thienyl, oxazolyl, thiazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrazinyl, pyrimidinyl, imidazothiazolyl, benzofuryl, benzothienyl, indolyl, oxoindolinyl, dioxoindolinyl, benzoxazolyl, oxobenzoxazolyl, benzothiazolyl, oxobenzthiazolyl, benzimidazolyl, oxobenzimidazolyl, benzofurazanyl, benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl, thiazolopyridyl, oxodihydrothiazolopyridyl, chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl, isoquinolyl, oxodihydroquinolyl, tetrahydroquinolyl, oxotetrahydroquinolyl, benzodioxanyl, quinazolinyl, acridinyl, oxodihydroacridinyl, phenothiazinyl, dihydrodibenzoxepinyl, benzocycloheptathienyl, dihydrothienobenzothiepinyl, dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl, dihydrodibenzazepinyl, oxodihydrodibenzazepinyl, octahydrodibenzazepinyl, benzocycloheptapyridyl, oxobenzocycloheptapyridyl, and

di-hydrodibenzothiazepinyl, bound directly or over a methylene group,

D/
cont
 R^{13} is selected from the group consisting of hydrogen, methyl, benzyl and phenyl,

C1
 R^{14} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl, naphthyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, indolyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl and tetrahydroquinolyl, bound directly or over a methylene group,

wherein in the formula



(G2b)

$\text{---NR}^{12}\text{R}^{14}$ may be selected from pyrrolidine, piperidine, hexahydroazepine, morpholine, 2,5-diazabicyclo[2.2.1]heptane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydroacridanone, (5H)-dihydrodibenzazepine, (11H)-dihydrodibenzo[b,e]oxazepine and (11H)-dihydrodibenzo[b,e]thiazepine,

wherein aromatic rings are substituted or unsubstituted, independently of each other, by one to three substituents which are independently selected from the group consisting of halogen, cyano, $\text{C}_1\text{--C}_6\text{-alkyl}$, trifluoromethyl, $\text{C}_3\text{--C}_8\text{-}$

D/ Cont
cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, a substituted C₁-C₆-alkoxy which is entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups on the aromatic ring or ring system may form an additional ring over a methylenedioxy bridge.

C1
46. (once amended) A compound according to claim 45, wherein:

R¹ is selected from the group consisting of hydrogen, fluorine, methyl, trifluoromethyl and hydroxy,

R² and

R³ are hydrogen,

R⁴ is hydrogen or hydroxy,

k is 0,

A is ethenylene or 1,3-butadienylene

D is selected from the group consisting of C₂-C₆-alkylene, C₂-C₆-alkenylene, a C₂-C₆-alkylene wherein the double bond is to ring E, and a C₂-C₆-alkenylene wherein the double bond is to ring E,

E is selected from the group consisting of pyrrolidine, piperidine, hexahydroazepine and morpholine,

G is selected from the group consisting of benzyl, phenethyl, fluorenylmethyl, anthrylmethyl,

B'
cont

CI

diphenylmethyl, fluorenyl, dihydrodibenzocycloheptenyl, furylmethyl, thienylmethyl, thiazolylmethyl, pyridylmethyl, benzothienylmethyl, quinolylmethyl, phenyl-thienylmethyl, phenyl-pyridylmethyl, dihydrodibenzoxepinyl, dihydrodibenzothiepinyl, acetyl, pivaloyl, phenylacetyl, diphenylacetyl, diphenylpropionyl, naphthylacetyl, benzoyl, naphthoyl, anthrylcarbonyl, oxofluorenylcarbonyl, oxodihydroanthrylcarbonyl, dioxodihydroanthrylcarbonyl, furoyl, pyridylcarbonyl, chromonylcarbonyl, quinolylcarbonyl, naphthylaminocarbonyl, dibenzylaminocarbonyl, benzylphenylaminocarbonyl, diphenylaminocarbonyl, indolyl-1-carbonyl, dihydrodibenzazepin-N-carbonyl, tetrahydroquinolyl-N-carbonyl, tetrahydrobenzo[b]azepinyl-N-carbonyl, methanesulfonyl, phenylsulfonyl, p-toluenesulfonyl, naphthylsulfonyl, quinolinsulfonyl, and diphenylphosphinoyl,

wherein aromatic rings are substituted or unsubstituted independently of each other by one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, C₁-C₆-alkoxy, entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups in the ring or ring system may form an additional ring over a methylenedioxy bridge.

47. (once amended) A compound according to claim 4,

which is selected from the group consisting of

N-[4-(1-methylsulfonylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide,

N-{4-[1-(2-naphthylsulfonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide,

N-{4-[1-(2-naphthylsulfonyl)-piperidin-4-yl]-butyl}-5-(pyridin-3-yl)-2,4-pentadienoic acid amide,

N-{4-[1-(1-naphthylaminocarbonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide,

N-[4-(1-diphenylaminocarbonyl-piperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide,

N-[4-(1-diphenylaminocarbonyl-piperidin-4-yl)-butyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide,

N-{4-[1-(10,11-dihydrodibenzo[b,f]azepin-5-yl-carbonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, and

N-[4-(1-diphenylphosphinoyl-piperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide

or as a pharmaceutically acceptable acid addition salt thereof.

48. (once amended) A compound according to claim 42, which is selected from the group consisting of N-[4-(1-acetylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide,

N-[4-(1-diphenylacetyl-piperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide, N-{4-[1-(3,3-diphenylpropionyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, N-[4-(1-benzoylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide, N-[4-(1-benzoylpiperidin-4-yl)-butyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide, and N-{4-[1-(9-oxo-9H-fluoren-4-yl-carbonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, or as a pharmaceutically acceptable acid addition salt thereof.

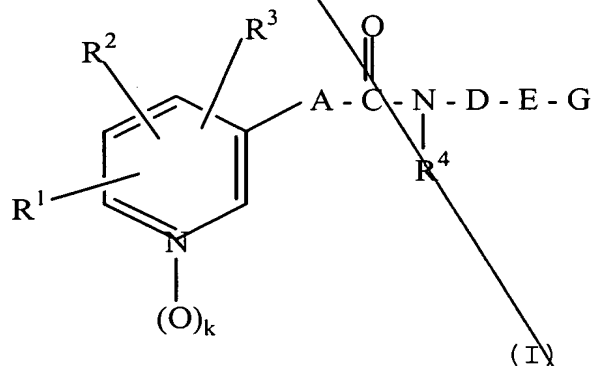
49. (once amended) A compound according to claim 42, which is selected from the group consisting of N-{4-[1-(phenylpyridin-3-yl-methyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, N-{4-[1-(phenylpyridin-4-yl-methyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, N-{4-[1-(6,11-dihydrodibenzo[b,e]oxepin-11-yl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide and N-{4-[1-(6,11-dihydrodibenzo[b,e]thiepin-11-yl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, or as a pharmaceutically acceptable acid addition salt thereof.

50. (once amended) A compound according to claim 42, which is selected from the group consisting of N-[7-(1-diphenylmethylnpiperidin-4-yl)-heptyl]-3-(pyridin-3-yl)-acrylamide, N-[8-(1-diphenylmethylnpiperidin-4-yl)-octyl]-3-(pyridin-3-yl)-acrylamide, N-[3-(1-diphenylmethylnpiperidin-4-yloxy)-propyl]-3-(pyridin-3-yl)-acrylamide, and N-[3-(1-benzylpiperidin-4-yloxy)-propyl]-3-(pyridin-3-yl)-acrylamide or as a pharmaceutically acceptable acid addition salt thereof.

51. (once amended) A compound according to claim 42,

c1
which is selected from the group consisting of N-[2-(1-diphenylmethylpiperidin-4-yl)-ethyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide, N-[4-(1-diphenylmethylpiperidin-4-yl)-butyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide, N-[5-(1-diphenylmethylpiperidin-4-yl)-pentyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide and N-[6-(1-diphenylmethylpiperidin-4-yl)-hexyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide or as a pharmaceutically acceptable acid addition salt thereof.

est
D2
c2
56. (once amended) A pharmaceutical composition comprising one or more of the compounds according to formula (I) and pharmaceutically acceptable salts of formula (I)



wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_4 -hydroxyalkyl, hydroxy, C_1 - C_4 -alkoxy, benzyloxy, C_2 - C_4 -alkanoyloxy, C_1 - C_4 -alkylthio, C_2 - C_5 -alkoxycarbonyl, aminocarbonyl, C_3 - C_9 -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6 , and bridged R^1R^2 ; wherein

R^5 is selected from the group consisting of hydrogen

and C₁-C₆-alkyl; and

R⁶ is selected from the group consisting of hydrogen and C₁-C₆-alkyl;

D²
cont
R² is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and hydroxy and bridged R¹R²;

C²
wherein

bridged R¹R² is where R¹R² are adjacent and form a bridge which is selected from the group consisting of -(CH₂)₄-, (CH=CH)₂- and -CH₂O-CR⁷R⁸-O-; wherein

R⁷ is selected from the group consisting of hydrogen, and C₁-C₆-alkyl; and

R⁸ is selected from the group consisting of hydrogen and C₁-C₆-alkyl;

R³ is selected from the group consisting of hydrogen, halogen and C₁-C₆-alkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano, or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted

once or twice by C_1 - C_3 -alkyl, fluorine, cyano, or phenyl,
1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted
by C_1 - C_3 -alkyl, fluorine, or cyano, and ethynylene;

D is selected from the group consisting of

C_1 - C_{10} -alkylene,

a substituted C_1 - C_{10} -alkylene which is substituted once or
twice by C_1 - C_3 -alkyl or hydroxy,

C_2 - C_{10} -alkenylene,

a substituted C_2 - C_{10} -alkenylene which is substituted once
or twice by C_1 - C_3 -alkyl or hydroxy,

a substituted C_2 - C_{10} -alkenylene which is substituted once
or twice by C_1 - C_3 -alkyl or hydroxy, wherein the double bond is
to E,

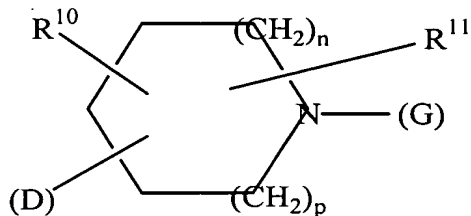
C_3 - C_{10} -alkynylene,

a substituted C_3 - C_{10} -alkynylene which is substituted once
or twice by C_1 - C_3 -alkyl or hydroxy,

an isosterically replaced C_1 to C_{10} group selected from
the group consisting of C_1 - C_{10} -alkylene, C_2 - C_{10} -alkenylene and
 C_3 - C_{10} -alkynylene, the isosterically replaced C_1 to C_{10} group
having methylene units and one to three of the methylene units
are isosterically replaced by O, S, NR^9 , CO, SO or SO_2 ; wherein

R^9 is selected from the group consisting of hydrogen, C_1 -
 C_3 -alkyl, C_2 - C_6 -acyl and methanesulfonyl;

E is



wherein **n** and **p** are, independent of each other, 0, 1, 2, or 3 wherein $n + p \leq 3$,

D² Cont
R¹⁰ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;

C²
R¹¹ is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, **G1**, **G2**, **G3**, **G4** and **G5**; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R¹² is selected from the group consisting of hydrogen,

C₁-C₆-alkyl,

C₃-C₆-alkenyl,

C₃-C₆-alkinyl,

C₃-C₈-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected

from the group consisting of N, S and O, which heterocycles are bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group;

R^{13} has the same meaning as R^{12} , but is selected independently thereof;

R^{14} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl,

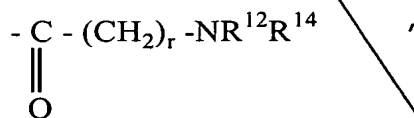
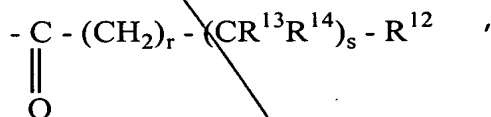
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or

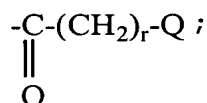
over a methylene group, and

D²
cont a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

C² G2 is selected from the group consisting of



and



wherein R¹² and R¹⁴ have the above meaning, and Q

is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N,

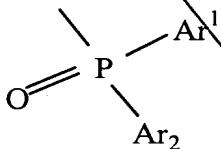
S and O,

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$,

G4 is



wherein

Ar^1 is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar^2 is selected from the group consisting of phenyl, pyridyl and naphthyl;

G5 is $-\text{COR}^{15}$,

wherein

R^{15} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy and benzyloxy; and

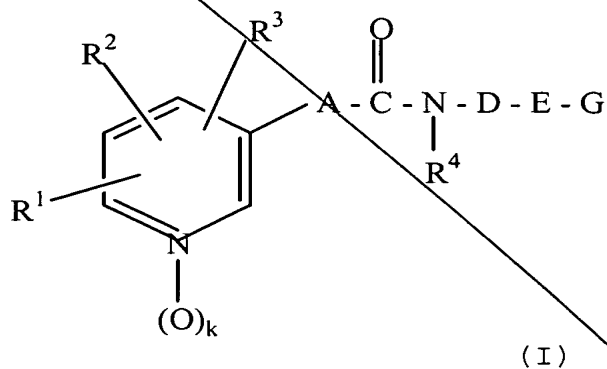
C2
D2
Cont

wherein aromatic rings in R^1 , R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q , Ar^1 and Ar^2 are unsubstituted or substituted, the substituted rings in R^1 , R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q , Ar^1 and Ar^2 having one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, phenyl, benzyl, hydroxy, C_1 - C_6 -alkoxy, and a substituted C_1 - C_6 -alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C_1 - C_6 -alkylthio, carboxy, C_1 - C_6 -alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono- C_1 - C_6 -alkylamino, and di- $(C_1$ - C_6 -alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C_1 - C_6 alkoxy may form an additional ring over a methylenedioxy bridge,

wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide.

push
D3
C3

64. (once amended) A method of inhibiting tumor cell growth in a human or animal body comprising administering to the human or animal body an effective amount of a pharmaceutical composition, wherein the pharmaceutical composition includes a compound of general formula (I)



wherein:

D³
cont

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_4 -hydroxyalkyl, hydroxy, C_1 - C_4 -alkoxy, benzyloxy, C_2 - C_4 -alkanoyloxy, C_1 - C_4 -alkylthio, C_2 - C_5 -alkoxycarbonyl, aminocarbonyl, C_3 - C_9 -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6 , and bridged R^1R^2 ; wherein

C³

R^5 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl; and

R^6 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, C_1 - C_6 -alkyl, trifluoromethyl and hydroxy and bridged R^1R^2 ;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen, and C_1 - C_6 -alkyl; and

R^8 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl;

R^3 is selected from the group consisting of hydrogen, halogen and C_1 - C_6 -alkyl;

R^4 is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, hydroxy, C_1 - C_6 -alkoxy and benzyloxy;

k is 0 or 1,

D3
cont
A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano, or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

C3
a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, or cyano, and ethynylene;

D is selected from the group consisting of

C₁-C₁₀-alkylene,

a substituted C₁-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

C₂-C₁₀-alkenylene,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

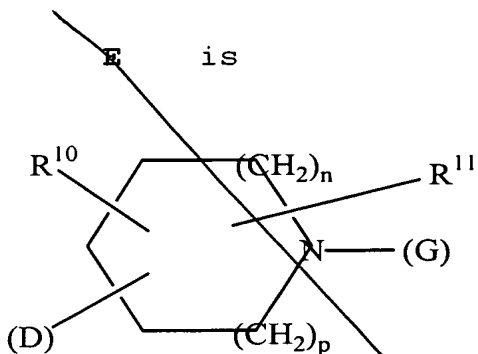
a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy, wherein the double bond is to E,

C₃-C₁₀-alkynylene,

a substituted C₃-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

an isosterically replaced C₁ to C₁₀ group selected from the group consisting of C₁-C₁₀-alkylene, C₂-C₁₀-alkenylene and C₃-C₁₀-alkynylene, the isosterically replaced C₁ to C₁₀ group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR⁹, CO, SO or SO₂; wherein

R⁹ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, C₂-C₆-acyl and methanesulfonyl;



wherein n and p are, independent of each other, 0, 1, 2, or 3 wherein $n + p \leq 3$,

R^{10} is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;

R^{11} is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, G1, G2, G3, G4 and G5; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of

Q3
cont

hydrogen,
C₁-C₆-alkyl,
C₃-C₆-alkenyl,
C₃-C₆-alkinyl,
C₃-C₈-cycloalkyl,
benzyl,
phenyl,

C3

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, which heterocycles are bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group;

R¹³ has the same meaning as R¹², but is selected independently thereof;

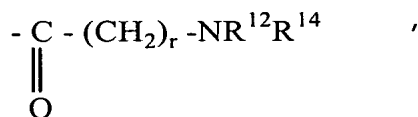
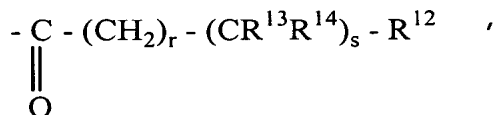
R¹⁴ is selected from the group consisting of hydrogen,
hydroxy,
methyl,
benzyl,
phenyl,

monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

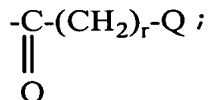
an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

G2 is selected from the group consisting of



and



wherein R^{12} and R^{14} have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

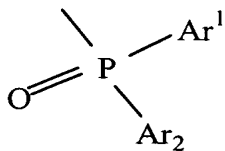
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$,

G4 is



wherein

Ar^1 is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar^2 is selected from the group consisting of

phenyl, pyridyl and naphthyl;

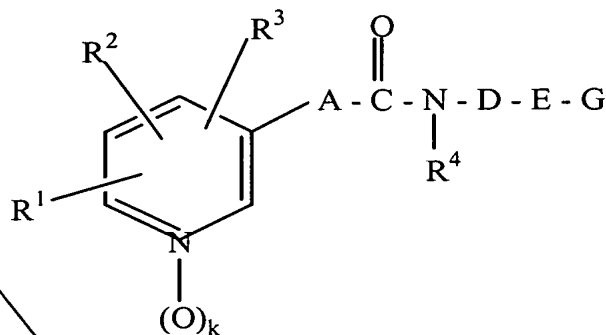
D3 cont
G5 is -COR¹⁵,

wherein

C3
R¹⁵ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy and benzyloxy; and

wherein aromatic rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² are unsubstituted or substituted, the substituted rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² having one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, and a substituted C₁-C₆-alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆ alkoxy may form an additional ring over a methylenedioxy bridge.

65. (Once amended) A method of suppressing autoimmune disease in a human or animal body comprising administering to the human or animal body an effective amount of a pharmaceutical composition of, wherein the pharmaceutical composition includes a compound of general formula (I) or a pharmaceutically acceptable salt of formula (I)



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_4 -hydroxyalkyl, hydroxy, C_1 - C_4 -alkoxy, benzyloxy, C_2 - C_4 -alkanoyloxy, C_1 - C_4 -alkylthio, C_2 - C_5 -alkoxycarbonyl, aminocarbonyl, C_3 - C_9 -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6 , and bridged R^1R^2 ; wherein

R^5 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl; and

R^6 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, C_1 - C_6 -alkyl, trifluoromethyl and hydroxy and bridged R^1R^2 ;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen,

and C₁-C₆-alkyl; and

R⁸ is selected from the group consisting of hydrogen and C₁-C₆-alkyl;

93
ant
R³ is selected from the group consisting of hydrogen, halogen and C₁-C₆-alkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

C3
k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano, or phenyl, C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, or cyano, and ethynylene;

D is selected from the group consisting of

C₁-C₁₀-alkylene,

a substituted C₁-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

C₂-C₁₀-alkenylene,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy, wherein the double bond is to E,

D3
cont

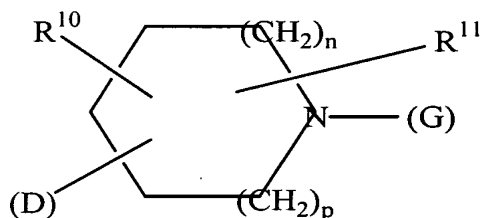
C₃-C₁₀-alkynylene,
a substituted C₃-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

an isosterically replaced C₁ to C₁₀ group selected from the group consisting of C₁-C₁₀-alkylene, C₂-C₁₀-alkenylene and C₃-C₁₀-alkynylene, the isosterically replaced C₁ to C₁₀ group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR⁹, CO, SO or SO₂; wherein

C3

R⁹ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, C₂-C₆-acyl and methanesulfonyl;

E is



wherein **n** and **p** are, independent of each other, 0, 1, 2, or 3 wherein **n + p ≤ 3**,

R¹⁰ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;

R¹¹ is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, G1, G2, G3, G4 and G5; wherein

D3
cont

G_1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

C3

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of
hydrogen,

C_1 - C_6 -alkyl,

C_3 - C_6 -alkenyl,

C_3 - C_6 -alkinyl,

C_3 - C_8 -cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles
which heterocycles contain one to three hetero-atoms selected
from the group consisting of N, S and O, which heterocycles
are bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially
hydrogenated carbocyclic ring system with 8 to 16 ring atoms
and at least one aromatic ring and the carbocyclic ring and
aromatic ring being bonded with a bond which is either over an
aromatic or a hydrogenated ring and either directly or over a
methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or
partially hydrogenated heterocyclic ring systems with 8 to 16
ring atoms and at least one aromatic ring, wherein one to
three ring atoms are selected from N, S and O and the
carbocyclic ring and aromatic ring being bonded with a bond

which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group;

R^{13} has the same meaning as R^{12} , but is selected independently thereof;

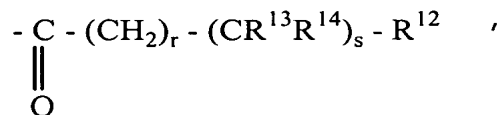
R^{14} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl,

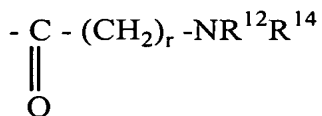
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

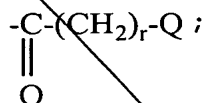
a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

G2 is selected from the group consisting of





and



wherein R^{12} and R^{14} have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

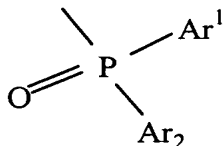
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $\text{-SO}_2\text{-(CH}_2\text{)}_r\text{-R}^{12}$,

G4 is



wherein

D3 cont
 Ar^1 is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar^2 is selected from the group consisting of phenyl, pyridyl and naphthyl;

C3
 G5 is $-\text{COR}^{15}$,

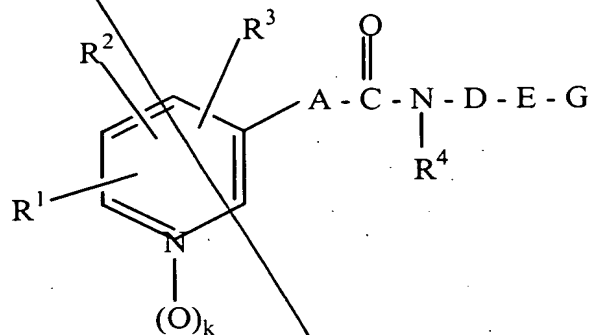
wherein

R^{15} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy and benzyloxy; and

wherein aromatic rings in R^1 , R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q , Ar^1 and Ar^2 are unsubstituted or substituted, the substituted rings in R^1 , R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q , Ar^1 and Ar^2 having one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, phenyl, benzyl, hydroxy, C_1 - C_6 -alkoxy, C_1 - C_6 -alkoxy, and a C_1 - C_6 alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C_1 - C_6 -alkylthio, carboxy, C_1 - C_6 -alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono- C_1 - C_6 -alkylamino, and di- $(\text{C}_1$ - C_6 -alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C_1 - C_6 alkoxy may form an additional ring over a methylenedioxy bridge.

Please add the following new claims.

68. A compound of formula (I) and pharmaceutically acceptable salts of formula (I)



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, fluorine, chlorine, bromine, methyl, trifluoromethyl and hydroxy,

R^2 and R^3 are hydrogen,

R^4 is hydrogen or hydroxy,

k is 0 or 1,

A is selected from the group consisting of C_2 - C_4 -alkenylene,

a substituted C_2 - C_4 -alkenylene which is substituted with fluorine,

1,3-butadienylene, and

a substituted 1,3-butadienylene which is substituted with fluorine,

D is selected from the group consisting of C_2 - C_6 -alkylene,

a C_2 - C_6 -alkenylene wherein the double bond is to E ,

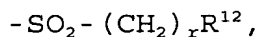
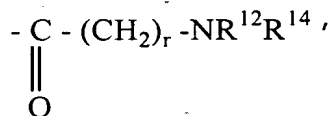
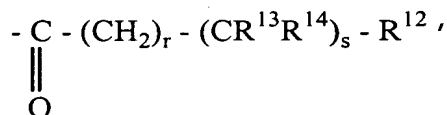
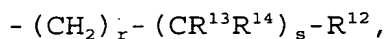
a substituted C_2 - C_6 -alkenylene which is substituted once

or twice by C₁-C₃-alkyl or hydroxy, and

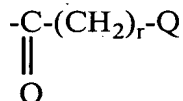
an isosterically replaced C₂-C₆-alkylene wherein a methylene unit of the alkenylene is isosterically replaced by O, NH, N(CH₃) or CO, or an ethylene group of the alkenylene is isosterically replaced by NH-CO or CO-NH, or a propylene group of the alkenylene is isosterically replaced by NH-CO-O or O-CO-NH,

E is selected from pyrrolidine, piperidine, 1,2,5,6-tetrahydropyridine, hexahydroazepine, morpholine and hexahydro-1,4-oxazepine,

G is selected from the group consisting of hydrogen, tert-butoxycarbonyl, diphenylphosphinoyl,



and



wherein r is 0 or 1, and

s is 0 or 1,

R¹² is selected from the group consisting of hydrogen,

D3
cont

C4

hydrogen, methyl, benzyl, phenyl, indenyl, oxoindanyl, naphthyl, tetrahydronaphthyl, fluorenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, and dibenzocycloheptenyl, dihydrodibenzocycloheptenyl, furyl, thienyl, oxazolyl, thiazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrazinyl, pyrimidinyl, imidazothiazolyl, benzofuryl, benzothienyl, indolyl, oxoindolinyl, dioxoindolinyl, benzoxazolyl, oxobenzoxazolinyl, benzothiazolyl, oxobenzthiazolinyl, benzimidazolyl, oxobenzimidazolinyl, benzofurazanyl, benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl, thiazolopyridyl, oxodihydrothiazolopyridyl, chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl, isoquinolyl, oxodihydroquinolinyl, tetrahydroquinolyl, oxotetrahydroquinolinyl, benzodioxanyl, quinazolinyl, acridinyl, oxodihydroacridinyl, phenothiazinyl, dihydrodibenzoxepinyl, benzocycloheptathienyl, dihydrothienobenzothiepinyl, dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl, dihydrodibenzazepinyl, oxodihydrodibenzazepinyl, octahydrodibenzazepinyl, benzocycloheptapyridyl, oxobenzocycloheptapyridyl, and dihydrodibenzothiazepinyl,

R¹³ is selected from the group consisting of hydrogen, methyl, benzyl or and phenyl,

R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl, and

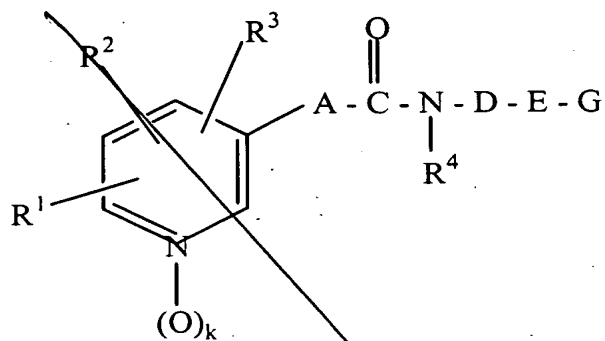
the group consisting of naphthyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, indolyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl and tetrahydroquinolyl,

wherein Q is selected from the group consisting of pyrrolidine, piperidine, hexahydroazepine, morpholine, 2,5-

C4
D³
Cont

~~diazabicyclo[2.2.1]heptane, indoline, isoindoline, (1H)-
dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-
tetrahydroisoquinoline, (1H)-tetrahydrobenzo[b]azepine, (1H)-
tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine,
(5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-
tetrahydroacridanone, (5H)-dihydrodibenzazepine, (11H)-
dihydrodibenzo[b,e]oxazepine and (11H)-
dihydrodibenzo[b,e]thiazepine, wherein general formula (I)
does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-
yl)ethyl]-2-propenamide.~~

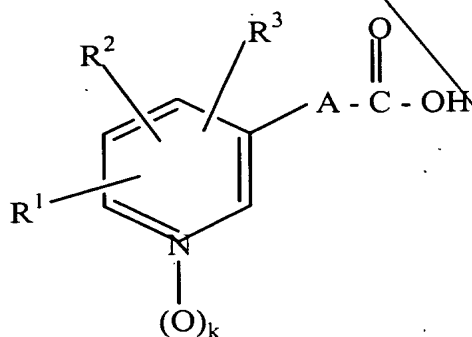
69. A method for the production of compounds having general formula (I)



(I)

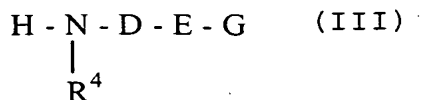
the method comprising:

reacting a carboxylic acids of formula (II)



(II)

with compounds of formula (III)



wherein

D3 cont
C4
 R^1 is selected from the group consisting of hydrogen, halogen, cyano, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl, $\text{C}_3\text{-C}_8\text{-cycloalkyl}$, $\text{C}_1\text{-C}_4\text{-hydroxyalkyl}$, hydroxy, $\text{C}_1\text{-C}_4\text{-alkoxy}$, benzyloxy, $\text{C}_2\text{-C}_4\text{-alkanoyloxy}$, $\text{C}_1\text{-C}_4\text{-alkylthio}$, $\text{C}_2\text{-C}_5\text{-alkoxycarbonyl}$, aminocarbonyl, $\text{C}_3\text{-C}_9\text{-dialkylaminocarbonyl}$, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6 , and bridged R^1R^2 wherein

R^5 is selected from the group consisting of hydrogen and $\text{C}_1\text{-C}_6\text{-alkyl}$, and

R^6 is selected from the group consisting of hydrogen and $\text{C}_1\text{-C}_6\text{-alkyl}$,

R^2 is selected from the group consisting of hydrogen, halogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl and hydroxy and bridged R^1R^2

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(\text{CH}_2)_4-$, $(\text{CH}=\text{CH})_2-$ and $-\text{CH}_2\text{O}-\text{CR}^7\text{R}^8-\text{O}-$, wherein

R^7 is selected from the group consisting of hydrogen, and $\text{C}_1\text{-C}_6\text{-alkyl}$ and

R^8 is selected from the group consisting of hydrogen and $\text{C}_1\text{-C}_6\text{-alkyl}$,

R^3 is selected from the group consisting of hydrogen, halogen and $\text{C}_1\text{-C}_6\text{-alkyl}$,

R^4 is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, hydroxy, C_1 - C_6 -alkoxy and benzyloxy,

k is 0 or 1,

D³ cont
 A is selected from the group consisting of C_2 - C_6 -alkenylene,

a substituted C_2 - C_6 -alkenylene which is substituted one to three-fold by C_1 - C_3 -alkyl, hydroxy, fluorine, cyano, or phenyl, C_4 - C_6 -alkadienylene,

C⁴
a substituted C_4 - C_6 -alkadienylene which is substituted once or twice by C_1 - C_3 -alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C_1 - C_3 -alkyl, fluorine, or cyano, and ethynylene,

D is selected from the group consisting of

C_1 - C_{10} -alkylene,

a substituted 1,3,5-hexatrienylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy,

C_2 - C_{10} -alkenylene,

a substituted C_2 - C_{10} -alkenylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy,

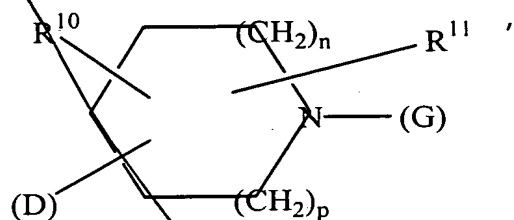
C_3 - C_{10} -alkynylene,

a substituted C_3 - C_{10} -alkynylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy,

an isosterically replaced C_1 to C_{10} group selected from the group consisting of C_1 - C_{10} -alkylene, C_2 - C_{10} -alkenylene and C_3 - C_{10} -alkynylene, the isosterically replaced C_1 to C_{10} group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR^9 , CO, SO or SO_2 , wherein

R^9 is selected from selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, C_2 - C_6 -acyl and methanesulfonyl,

E is



C4

wherein n and p are, independent of each other, 0, 1, or 2, wherein $n + p = 2$,

R^{10} is selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, hydroxy, hydroxymethyl, carboxy and C_2 - C_7 -alkoxycarbonyl,

R^{11} is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E,

G is selected from the group consisting of hydrogen, G1, G2, G3, G4 and G5, wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$
wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of hydrogen,
 C_1 - C_6 -alkyl,
 C_3 - C_6 -alkenyl,
 C_3 - C_6 -alkinyl,

C₃-C₈-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, the N, S and O being either bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carboxylic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group,

R¹³ has the same meaning as R¹², but is selected independently thereof,

R¹⁴ is selected from the group consisting of hydrogen, hydroxy,

methyl,

benzyl,

phenyl,

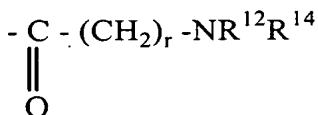
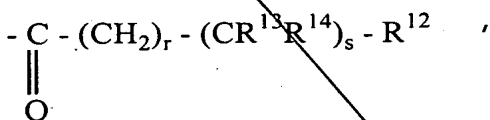
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms

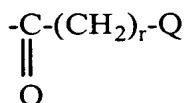
and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

D³ cont
a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group,

C4
G2 is selected from the group consisting of



and



wherein R^{12} and R^{14} have the above meaning, and Q

is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

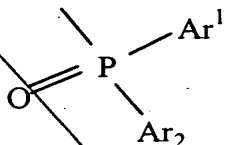
saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

and

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms,

G3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$,

G4 is



wherein

Ar^1 is selected from the group consisting of phenyl, pyridyl and naphthyl and

Ar^2 is selected from the group consisting of phenyl, pyridyl and naphthyl,

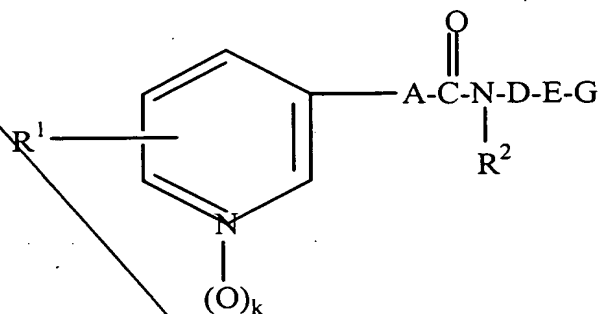
G5 is $-\text{COR}^{15}$,

wherein

R^{15} is selected from the group consisting of trifluoromethyl, $\text{C}_1\text{-C}_6\text{-alkoxy}$, $\text{C}_3\text{-C}_6\text{-alkenyloxy}$ and benzyloxy, and

wherein aromatic rings in R^1 , R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q, Ar^1 and Ar^2 are unsubstituted or substituted, the substituted rings in R^1 , R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q, Ar^1 and Ar^2 having one to three substituents which are independently selected from the group consisting of halogen, cyano, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl, $\text{C}_3\text{-C}_8\text{-cycloalkyl}$, phenyl, benzyl, hydroxy, and $\text{C}_1\text{-C}_6\text{-alkoxy}$.

70. A compound of formula (I) and pharmaceutically acceptable acid salts of formula I



wherein:

R¹ = H or F

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano, or phenyl, C₄-C₆-alkenylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, or cyano, and ethynylene;

R² is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

D is selected from the group consisting of C₁-C₁₀-alkylene,

a substituted 1,3,5-hexatrienylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

C_2-C_{10} -alkenylene,

a substituted C_2-C_{10} -alkenylene which is substituted once or twice by C_1-C_3 -alkyl or hydroxy,

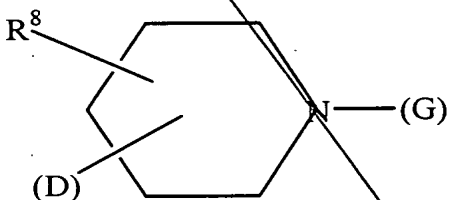
C_3-C_{10} -alkynylene,

a substituted C_3-C_{10} -alkynylene which is substituted once or twice by C_1-C_3 -alkyl or hydroxy,

an isoterically replaced C_1 to C_{10} group selected from the group consisting of C_1-C_{10} -alkylene, C_2-C_{10} -alkenylene and C_3-C_{10} -alkynylene, the isoterically replaced C_1 to C_{10} group having methylene units and one to three of the methylene units being isoterically replaced by O, S, NR^3 , CO SO or SO_2 ;

R^3 is selected from selected from the group consisting of hydrogen, C_1-C_3 -alkyl, C_2-C_6 -acyl and methanesulfonyl;

E is



G is selected from the group consisting of

$-(CH_2)_r-(CR^4R^6)_sR^5$,

$-C-(CH_2)_r-(CR^4R)_sR^6$,

\parallel

O

$-C-(CH_2)_r-NR^4R^6$,

\parallel

O

$-SO_2(CH_2)_rR^4$,



D3 cont
C4
 r=0, 1 or 2,

s=0 or 1,

R⁴ is selected from the group consisting of hydrogen, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₆ alkenyl, C₃-C₈-cycloalkyl, benzyl phenyl, and substituted phenyl which substituted phenyl is substituted with one to three substituents selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, and C₁-C₆-alkoxy;

R⁵ is selected from the group consisting of hydrogen, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₆ alkenyl, C₃-C₈-cycloalkyl, benzyl phenyl, and substituted phenyl which substituted phenyl is substituted with one to three substituents selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, and C₁-C₆-alkoxy;

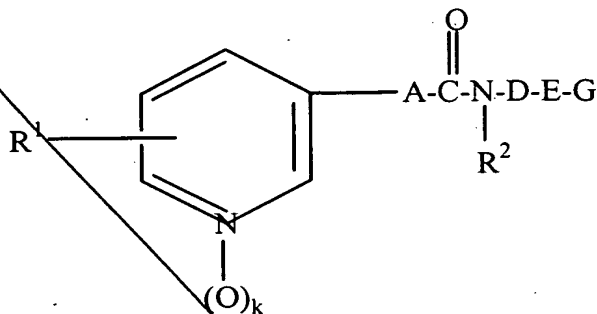
R⁶ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl;

R⁷ is selected from trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy and benzyloxy;

R⁸ is selected from the group consisting of C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;

and wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide.

71. A compound of formula (I) and pharmaceutically acceptable salts of formula (I)



C⁴
wherein:

R¹ is selected from the group consisting of hydrogen, fluorine, chlorine, methoxy, methyl, and hydroxy;

R² and R³ are hydrogen;

R⁴ is hydrogen, methyl or hydroxy;

k is 0 or 1;

A is selected from the group consisting of C₂-C₄-alkenylene,

a substituted C₂-C₄-alkenylene which is substituted with fluorine, cyano, hydroxy and methyl,

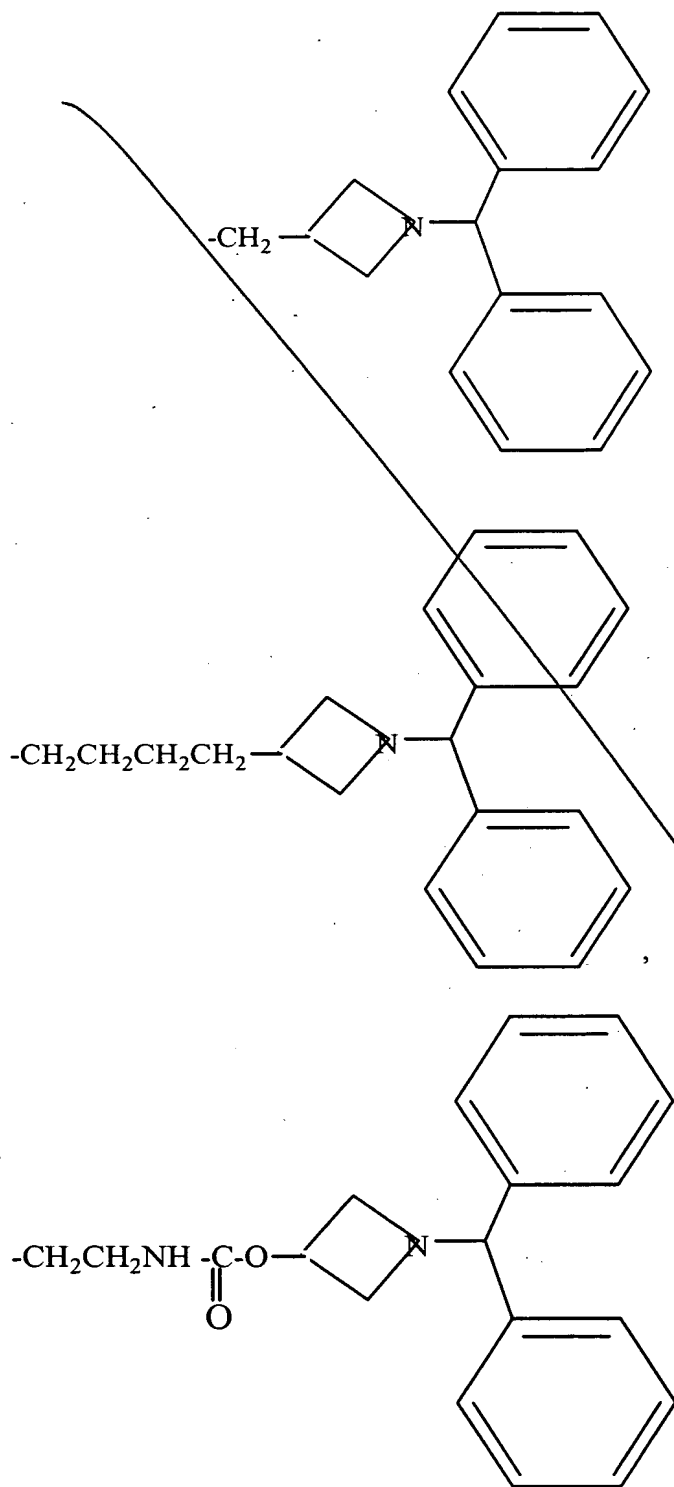
1,3-butadienylene, and

a substituted 1,3-butadienylene which is substituted with fluorine;

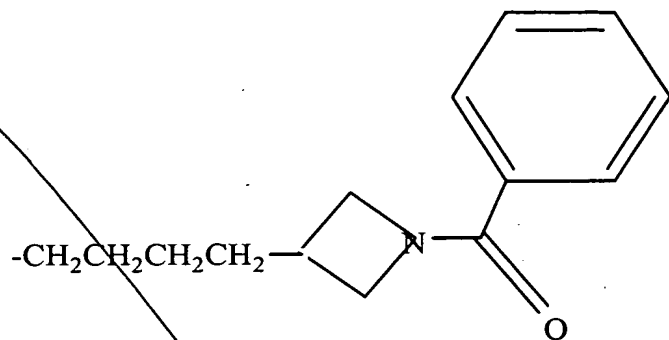
DEG when together form the structure selected from the group consisting of

D³
cont

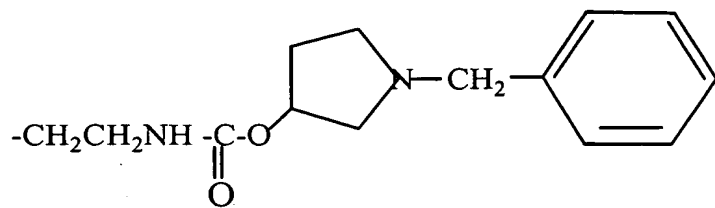
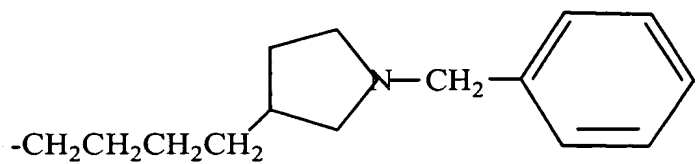
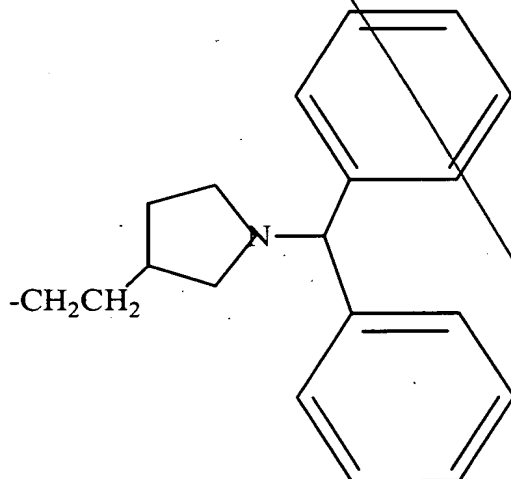
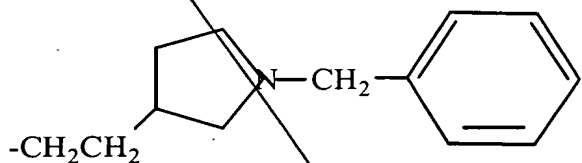
C4



D³
cont

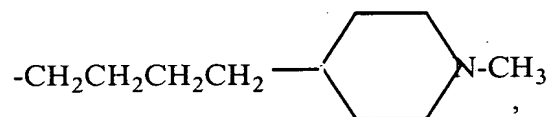
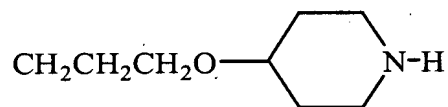
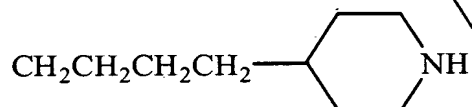
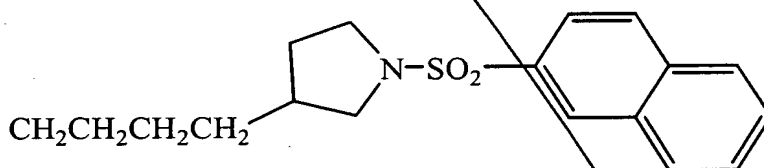
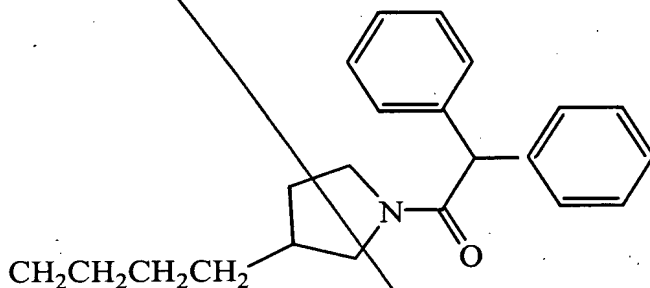
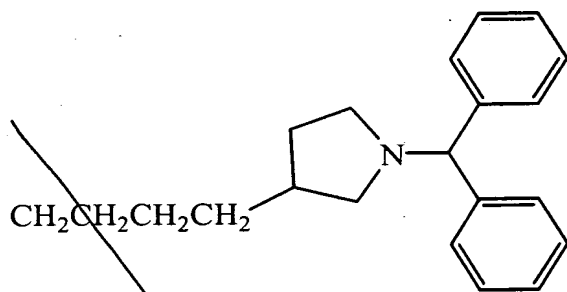


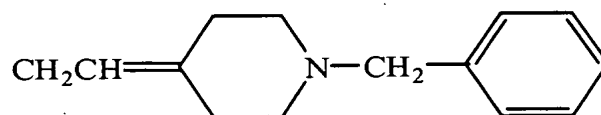
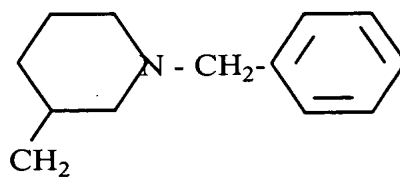
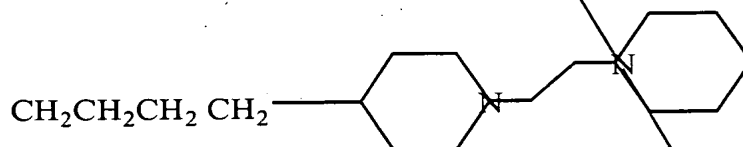
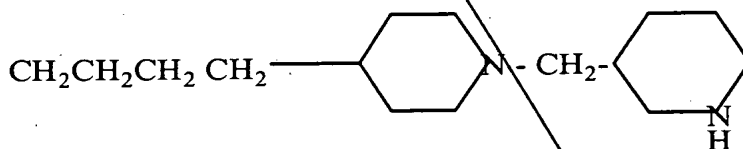
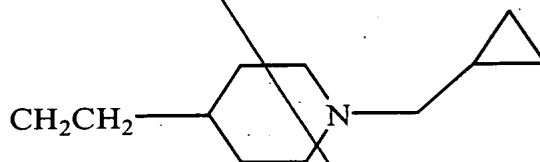
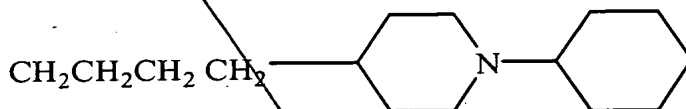
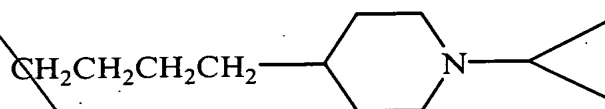
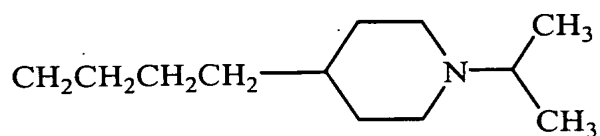
C4



D³
cont

C⁴

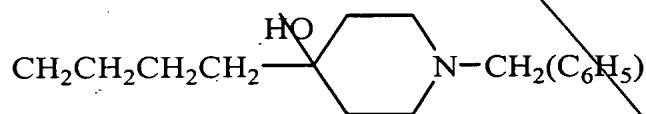
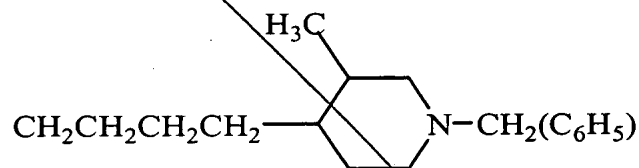
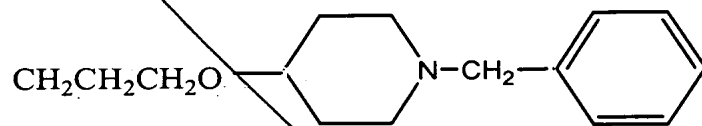
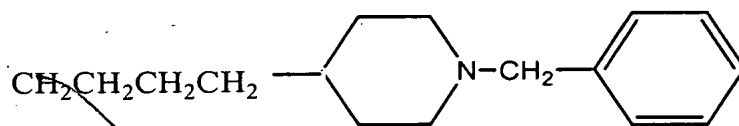




D³
cont

C4

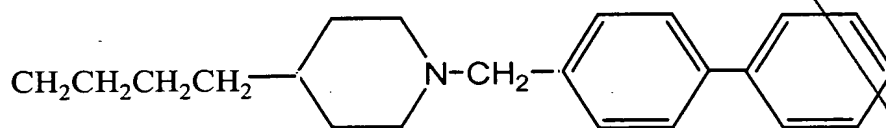
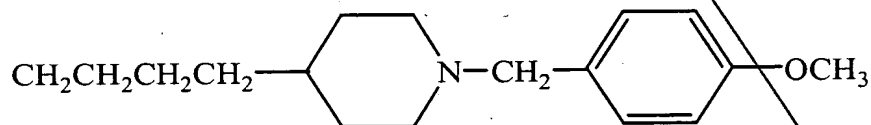
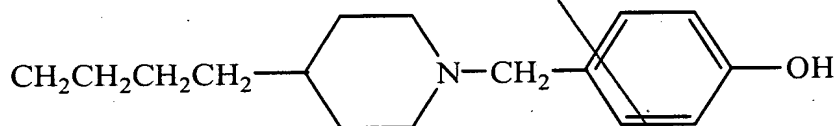
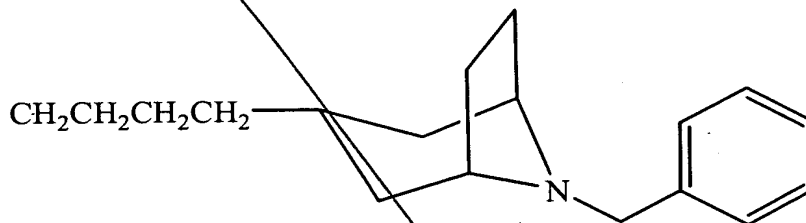
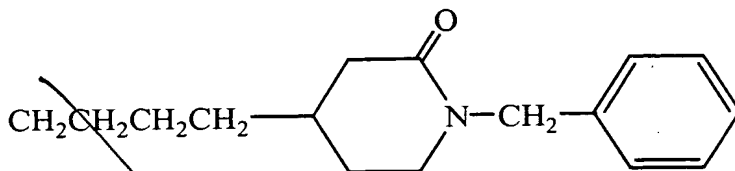
O³
cont



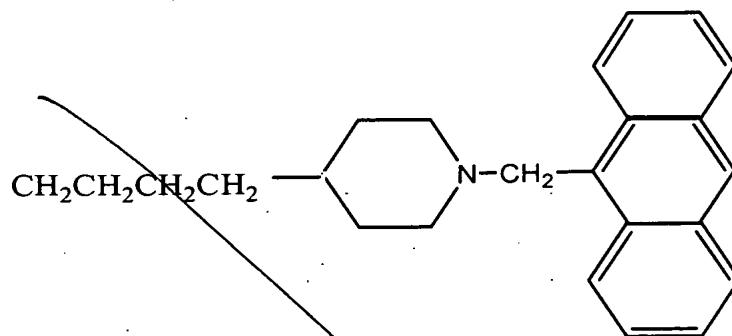
C4

D³
cont

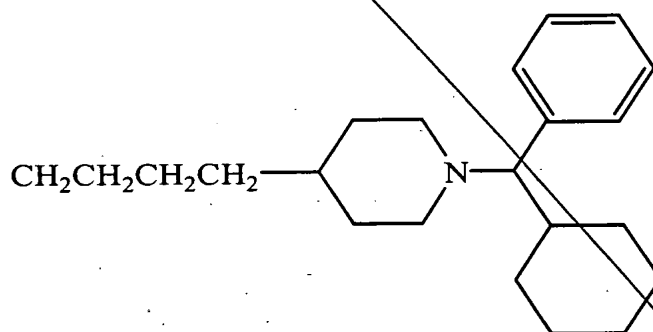
C4



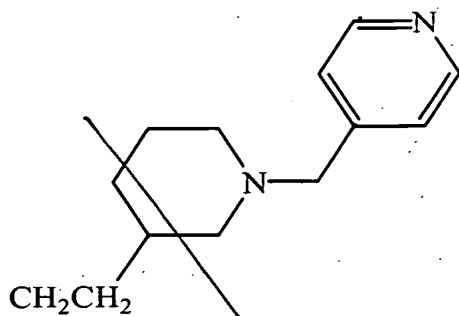
D³
cont



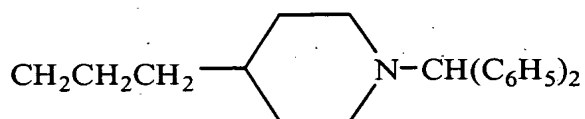
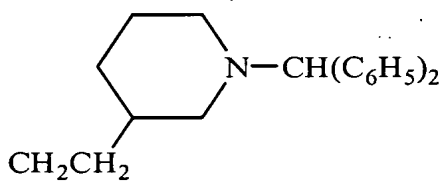
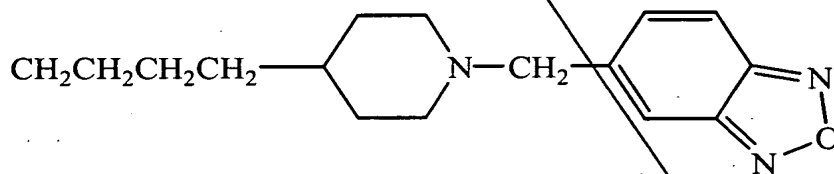
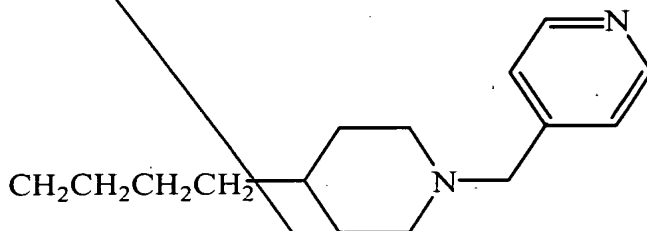
C4



D³
cont

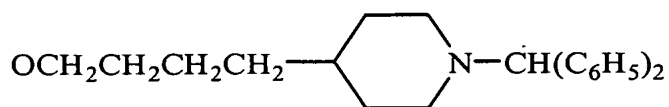
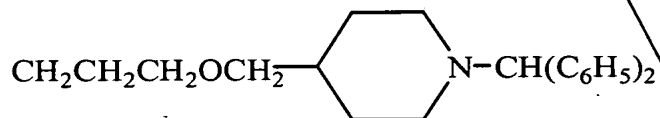
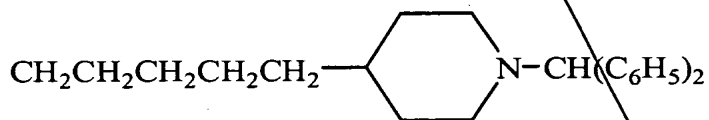
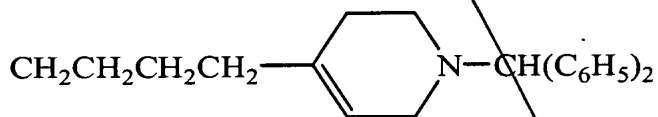
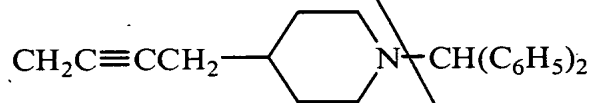
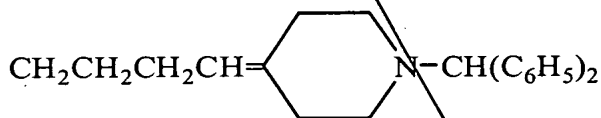
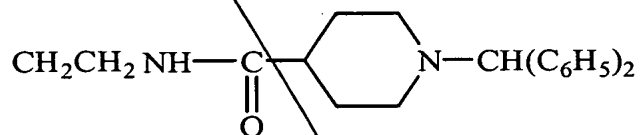
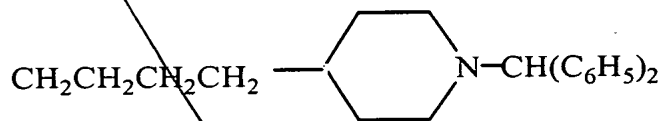
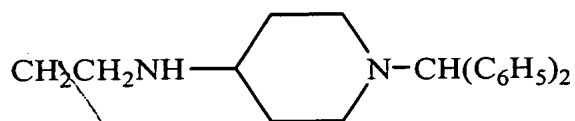


C4



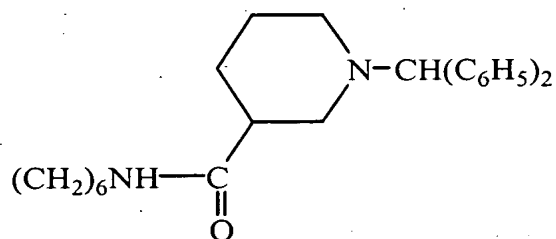
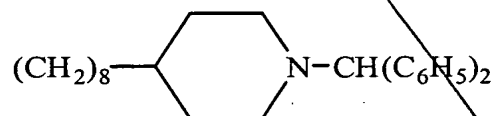
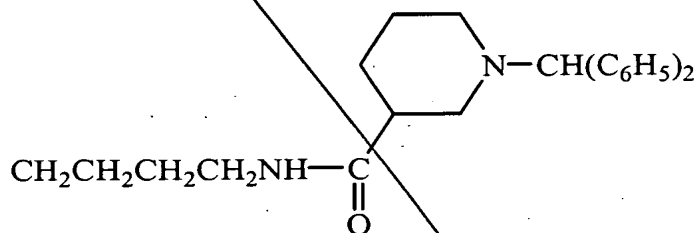
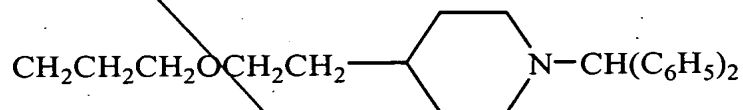
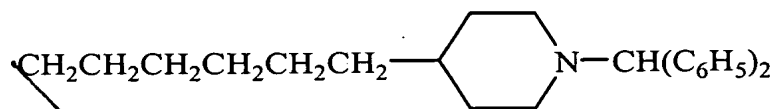
D³
cont

C4

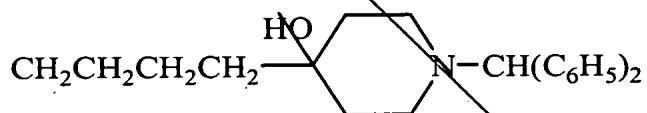
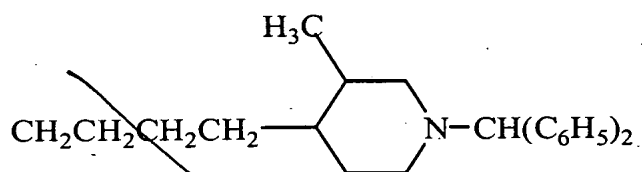


D³
cont

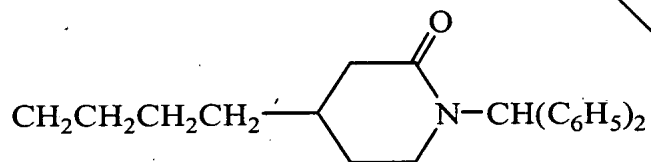
C4



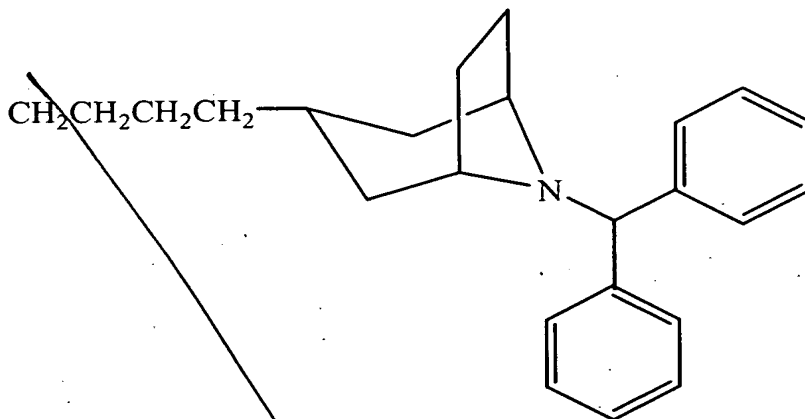
D³
cont



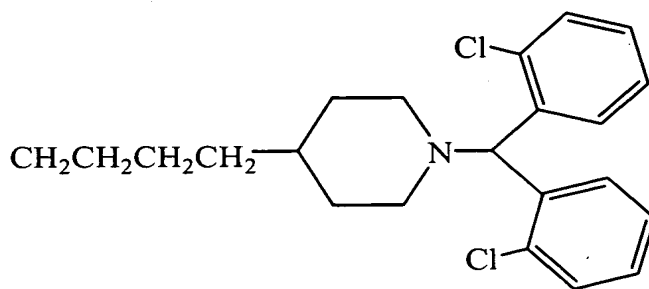
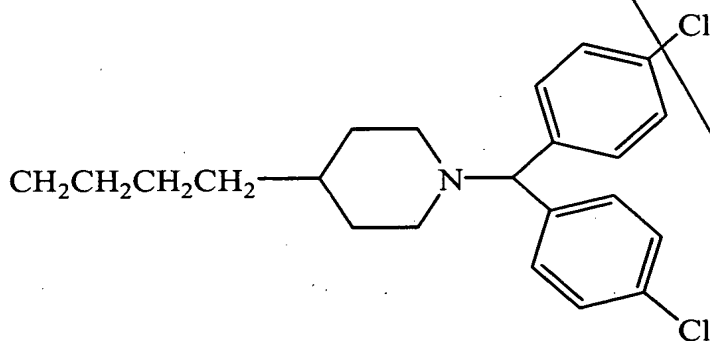
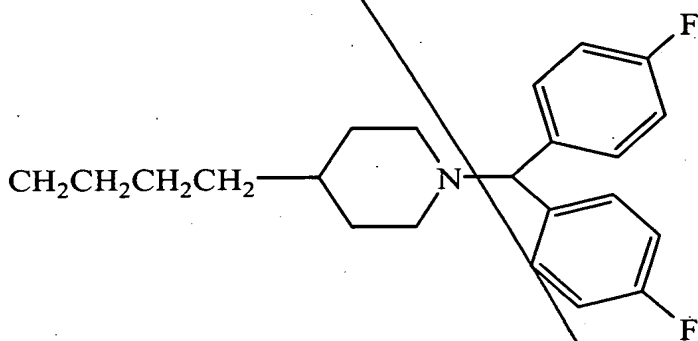
C4



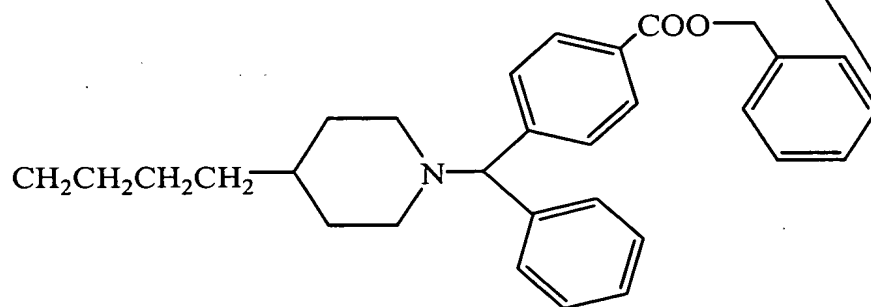
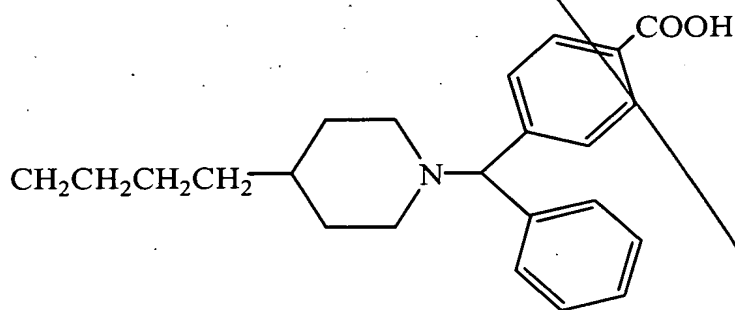
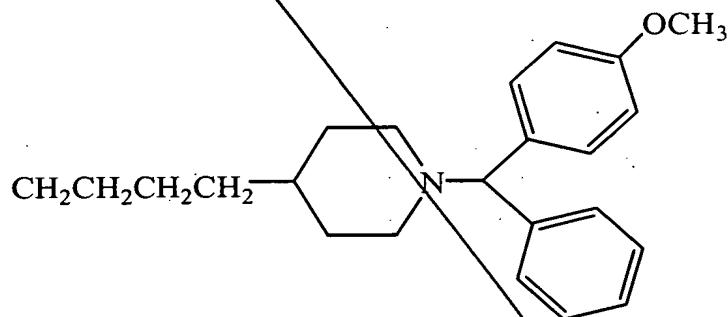
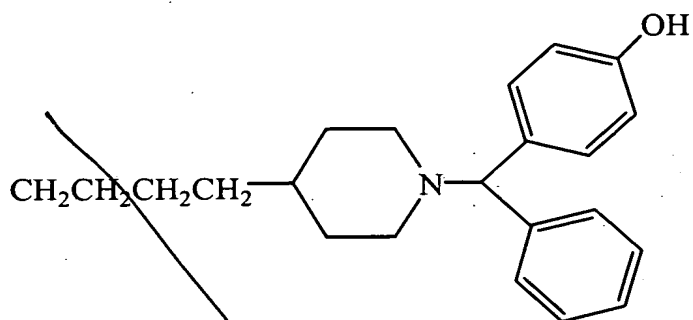
D³
cont



C4



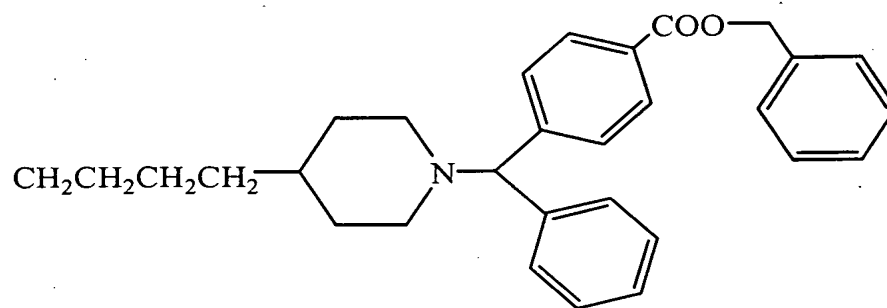
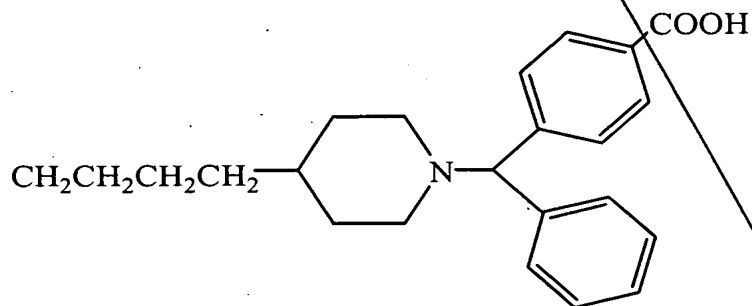
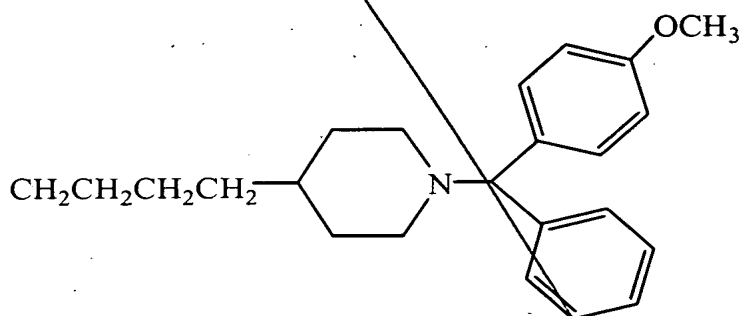
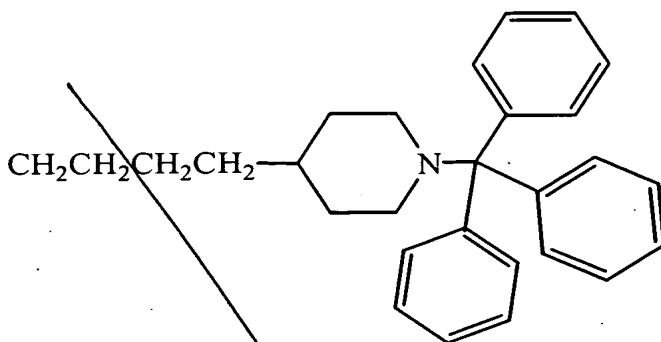
D³
Cont



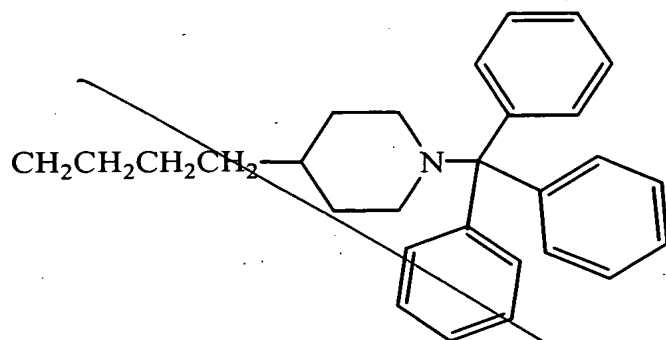
C4

D³
cont

C4

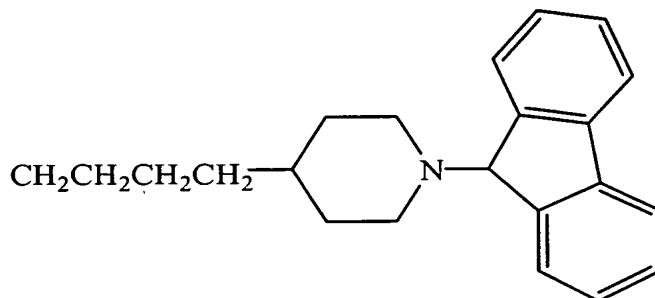
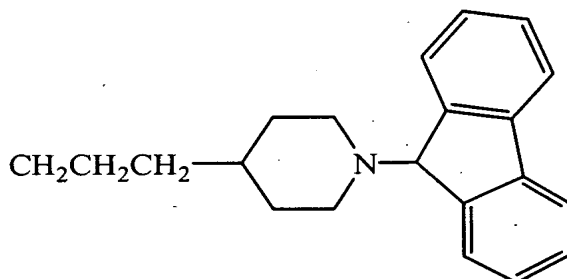
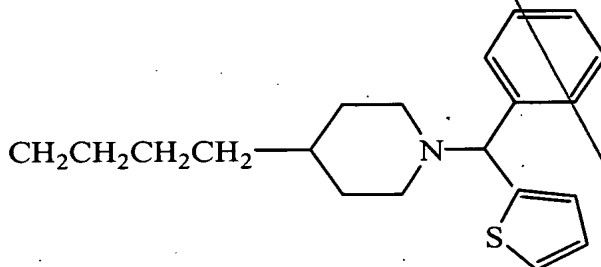
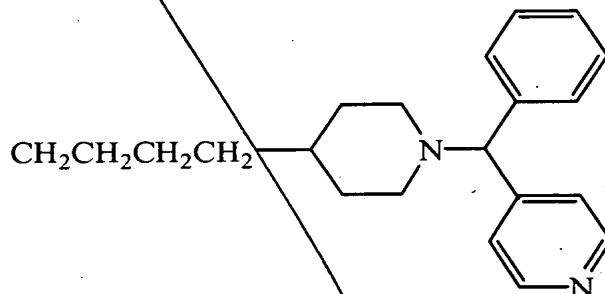
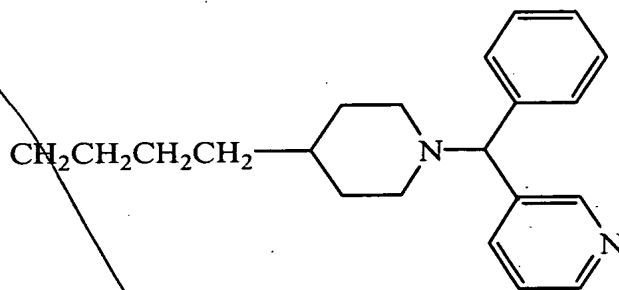


D³
cont

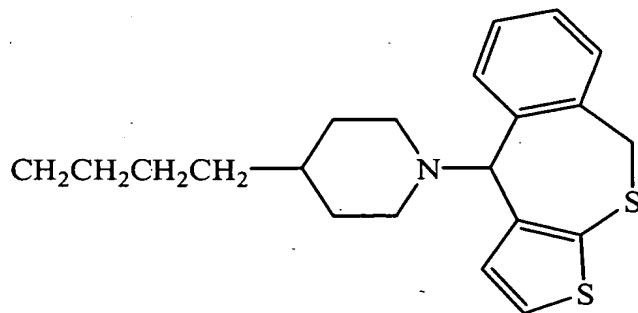
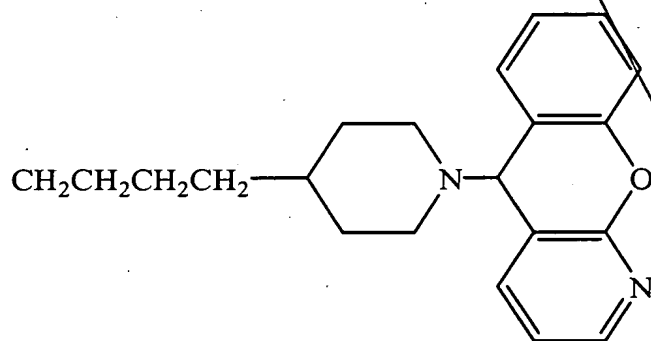
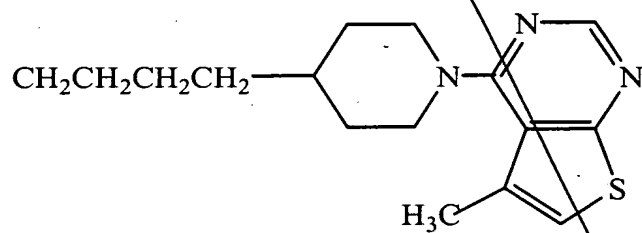
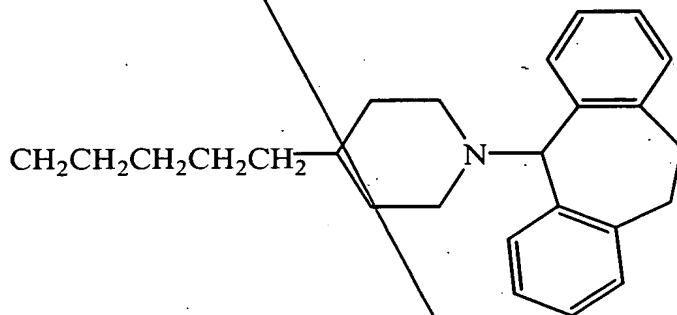
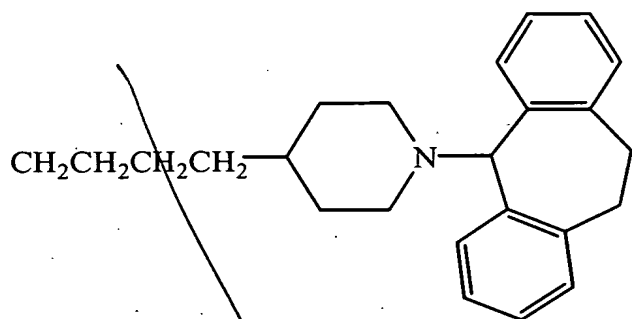


C4

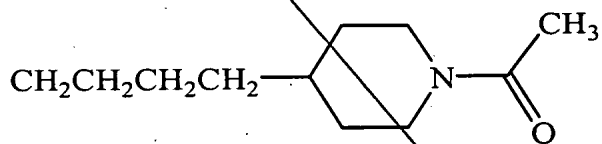
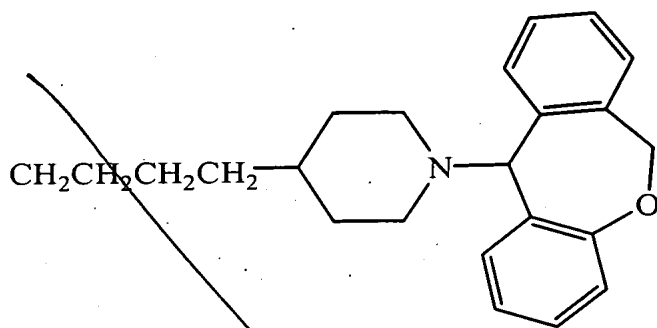
D³
cont



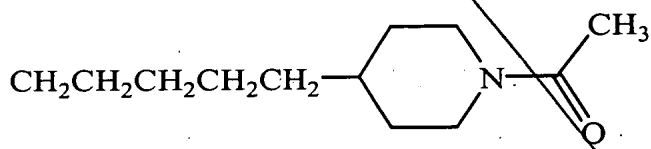
D3
cont



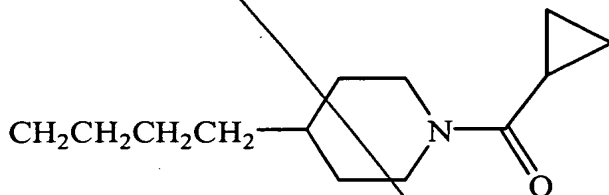
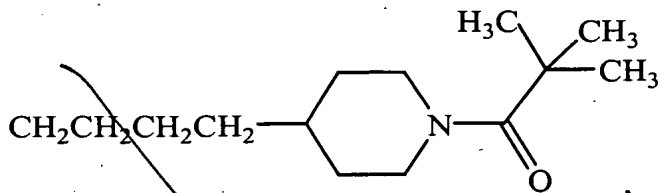
D³
cont



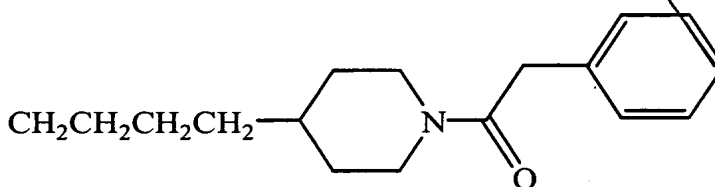
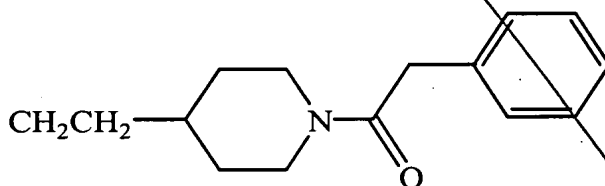
C4



D³
cont

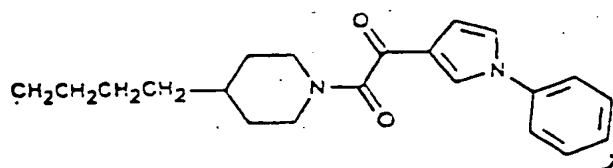
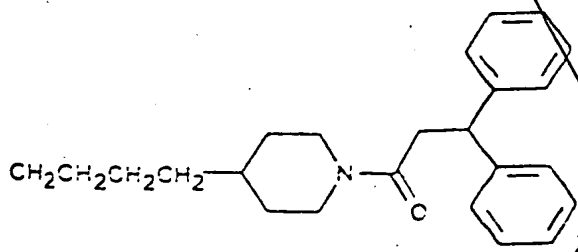
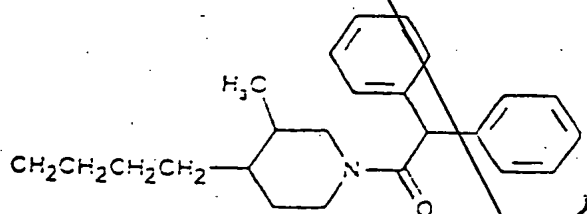
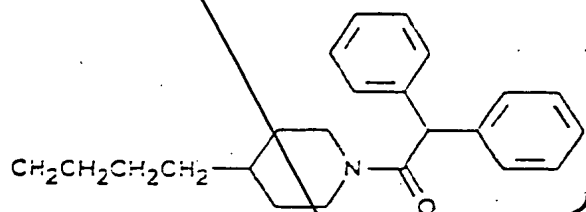
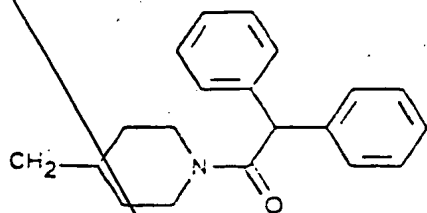


C4

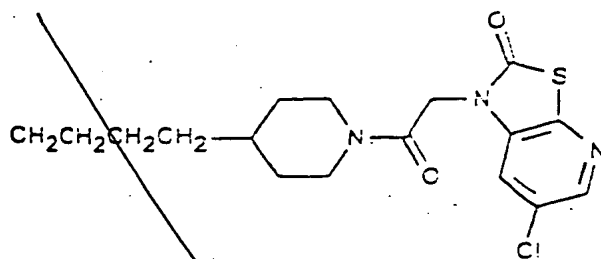


D3
cont

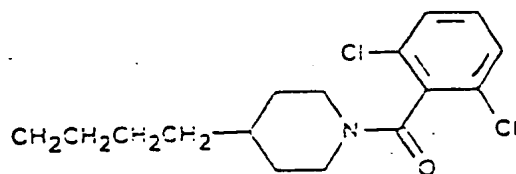
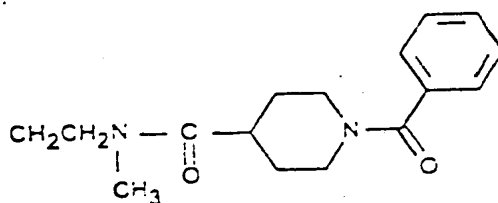
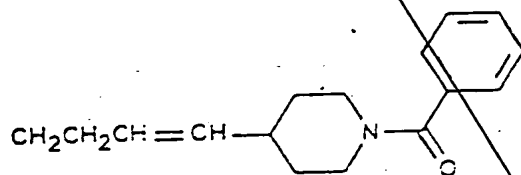
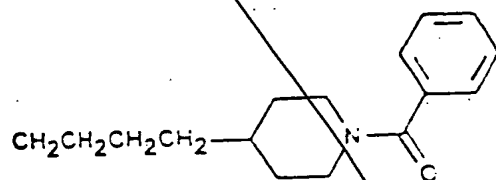
C4



D³
cont

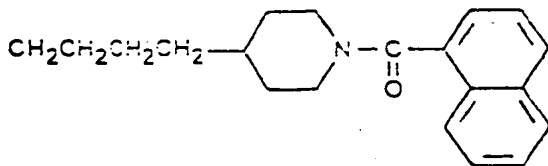
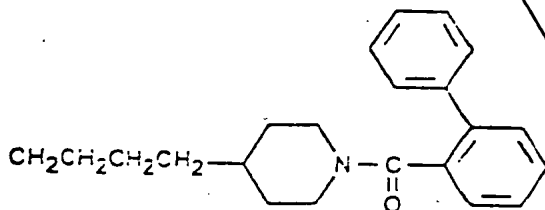
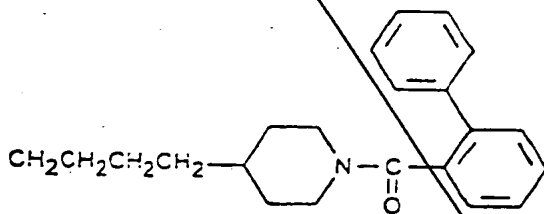
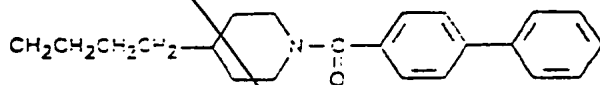
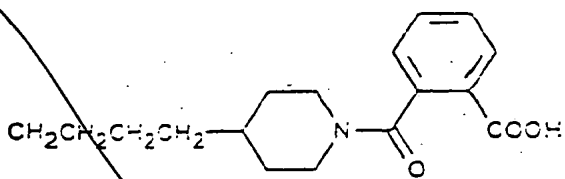


C4



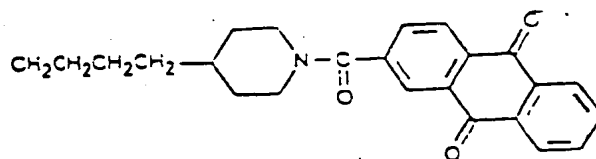
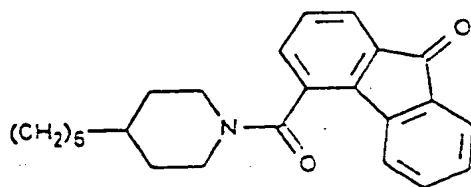
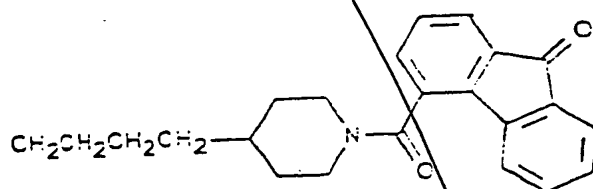
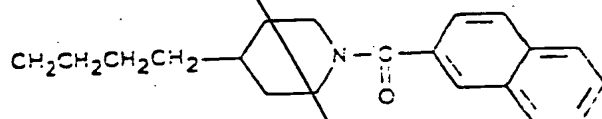
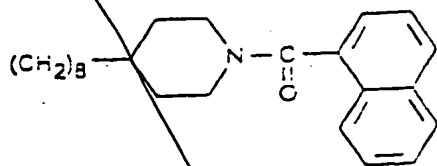
D³
cont

C4



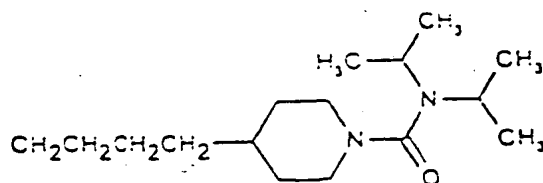
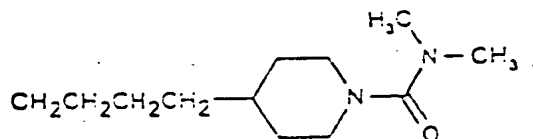
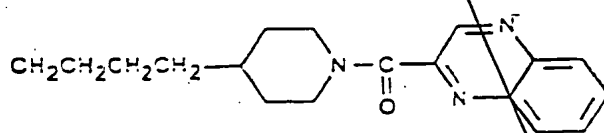
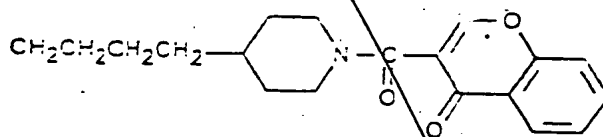
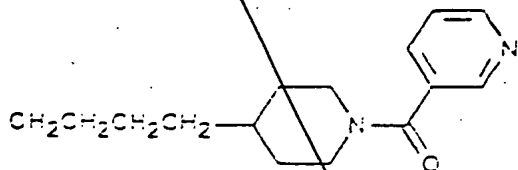
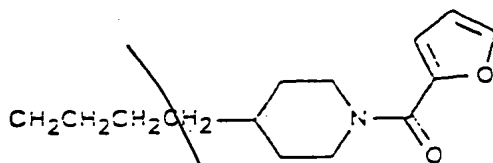
D³
cont

C4



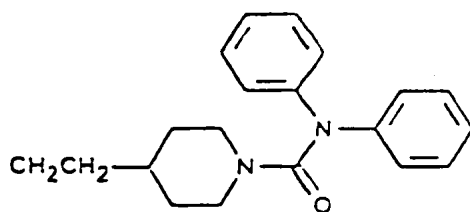
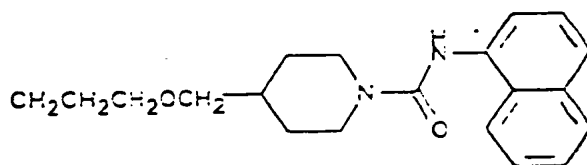
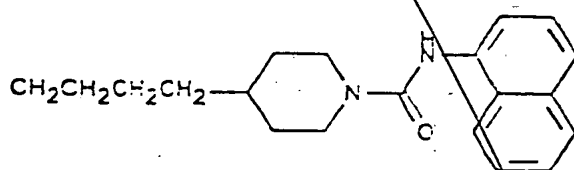
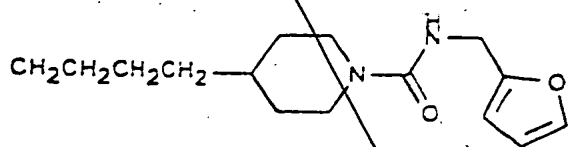
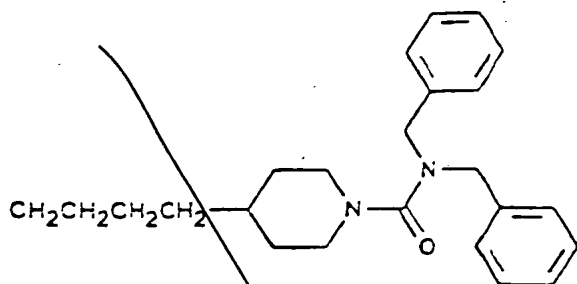
D³
cont

C4



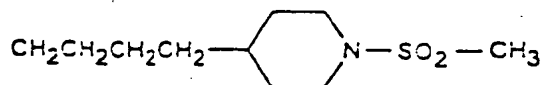
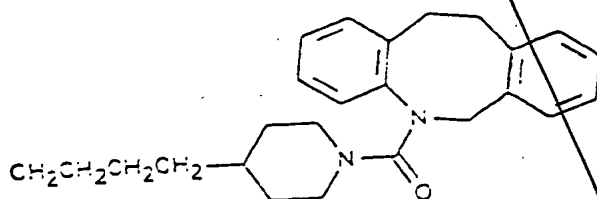
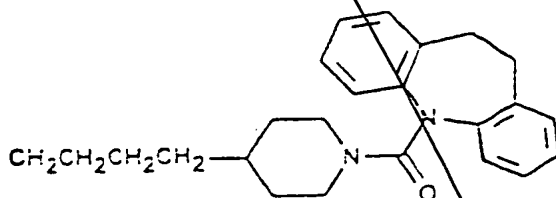
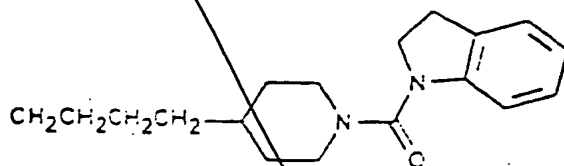
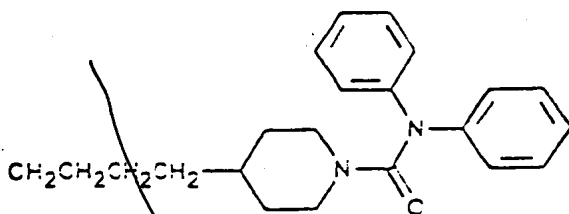
0³
cont

C4



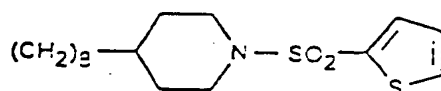
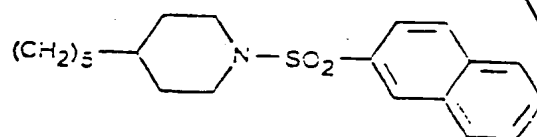
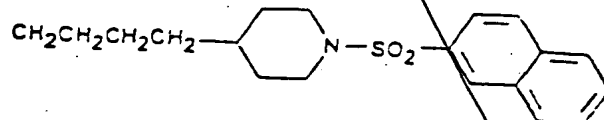
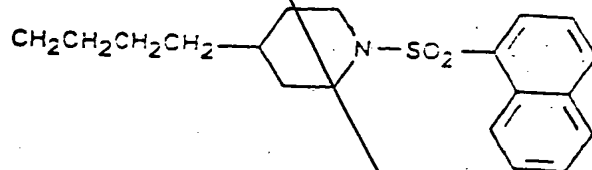
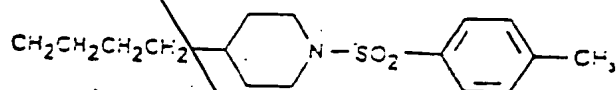
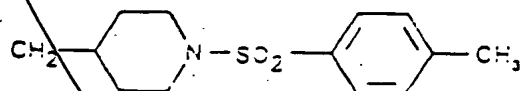
B³
cont

C4



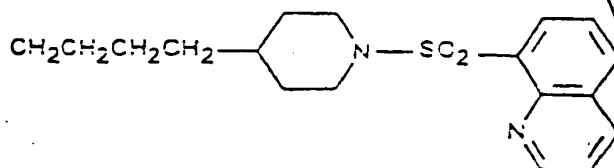
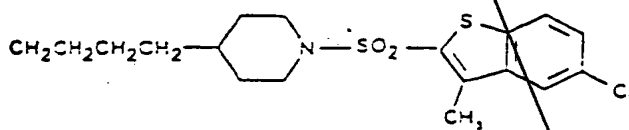
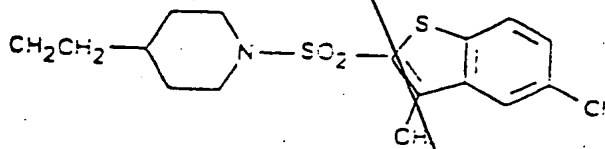
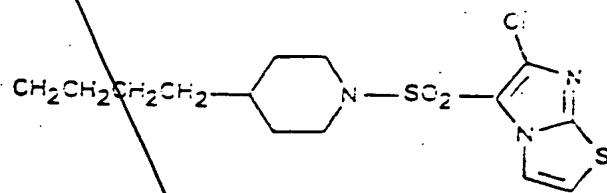
D³
cont

C4



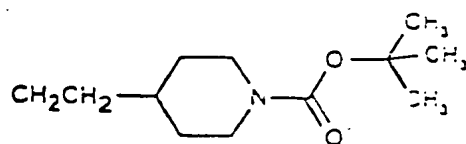
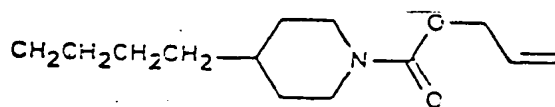
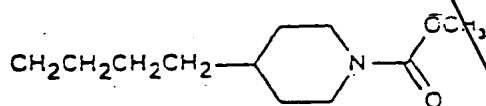
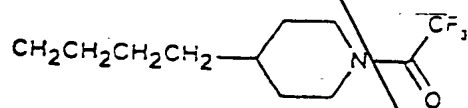
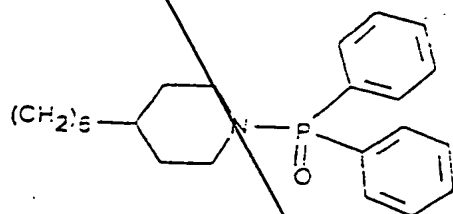
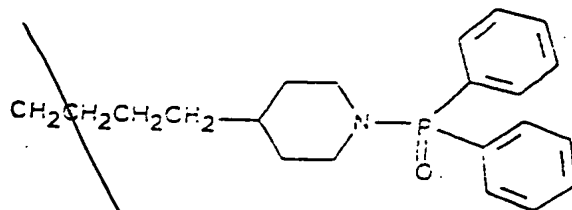
D³
cont

C4



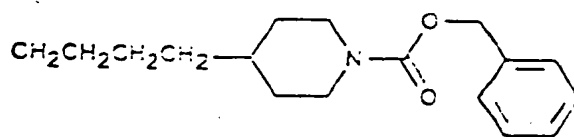
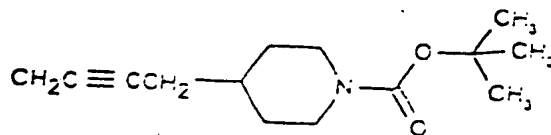
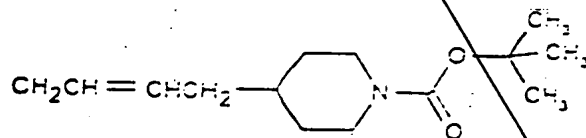
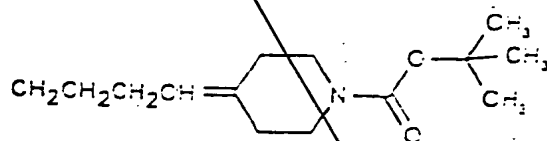
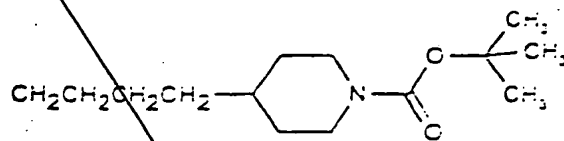
D³
cont

C4



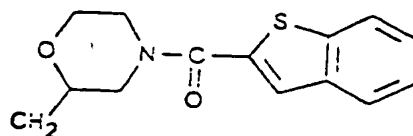
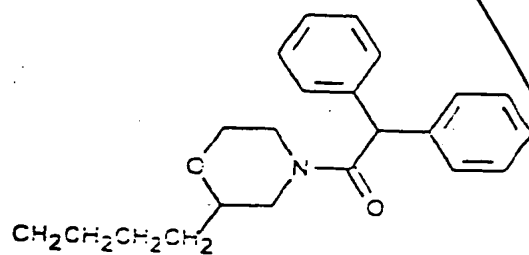
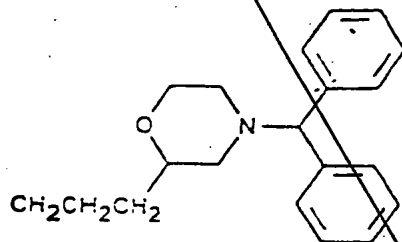
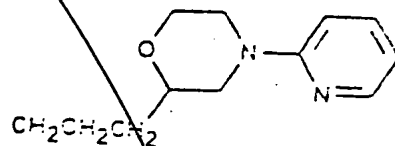
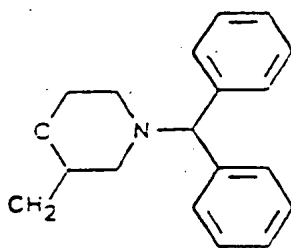
D³
cont

C4



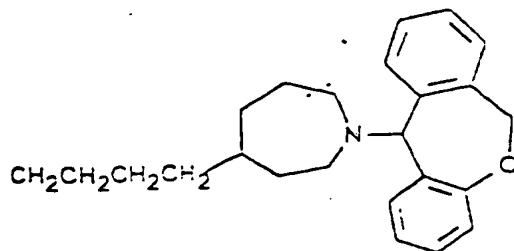
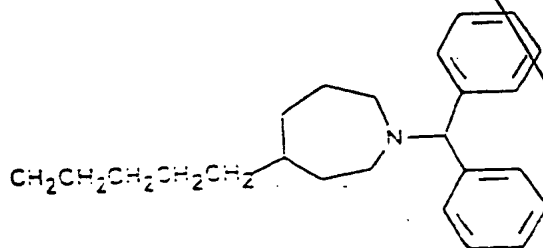
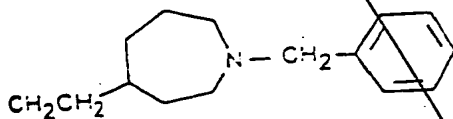
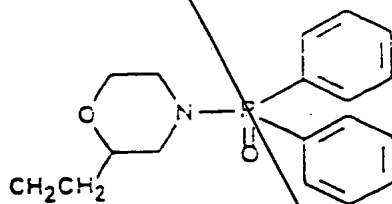
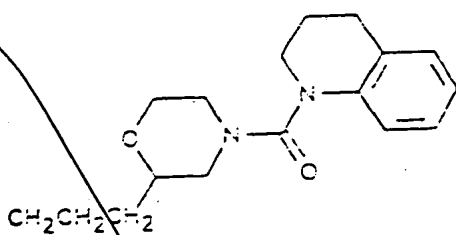
19³
cont

C4

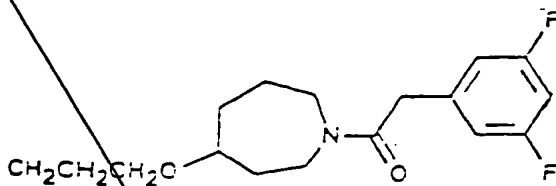


B³
cont

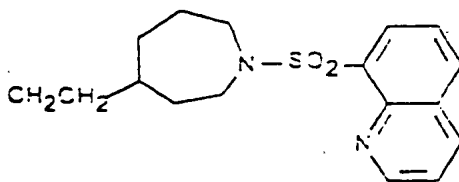
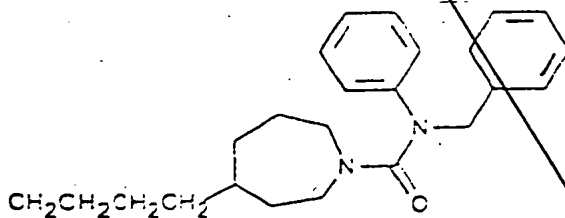
C4



19³
cont

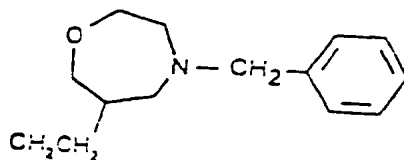
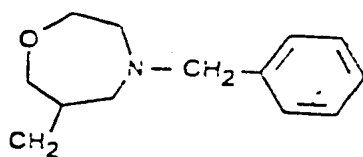
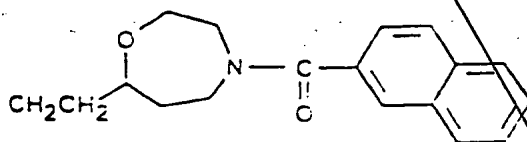
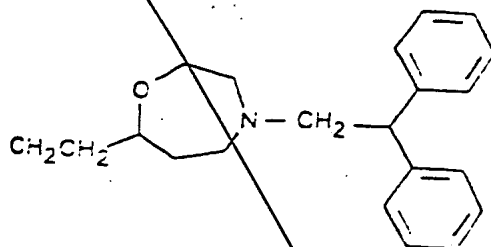
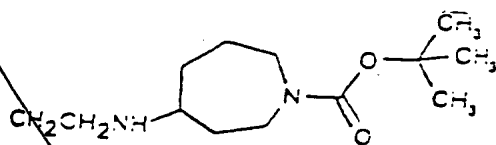


C4



103
cont

C4



D3
cont

72. A method of inhibiting tumor cell growth according to claim 64, wherein the composition is administered by a method selected from the group consisting of subcutaneously, intramuscularly, intravenously, intracutaneous, orally, sublingually, transdermally, topically and combinations thereof.

C4

73. A method of inhibiting tumor cell growth according to claim 64, wherein the composition is administered in combination with compounds selected from the group consisting of cytostatic agents, DNA intercalating substances, topoisomerase inhibitors, spindle poisons, hormonally active agents, and mixtures thereof.

74. A method of inhibiting tumor cell growth according to claim 64, wherein cytostatic agents are selected from the group consisting of

L-asparaginase, bleomycin, hydroxyurea, P-glycoprotein, MRP, glutathione-S-transferase, metallothionein, and mixtures thereof;

antimetabolites selected from the group consisting of cytarabine, 5-fluorouracil, 6-mercaptopurine, methotrexate, and mixtures thereof;

alkylating agents selected from the group consisting of busulfan, carmustine, cisplatin, caroplatin, cyclophosphamide, dacarbazine, melphalan, thiotepa, and mixtures thereof;

DNA intercalating substances and topoisomerases selected from the group consisting of actinomycin D, daunorubicin, doxorubicin, mitomycin D, mitoxantrone, etoposide, topotecan irinotecan, and mixtures thereof;

spindle poisons selected from the group consisting of vincristine, navelbin, taxol, taxoter, and mixtures thereof; and

hormonally active agents selected from the group consisting of tamoxifen, flutamide, formestane, goserelin, and mixtures thereof.

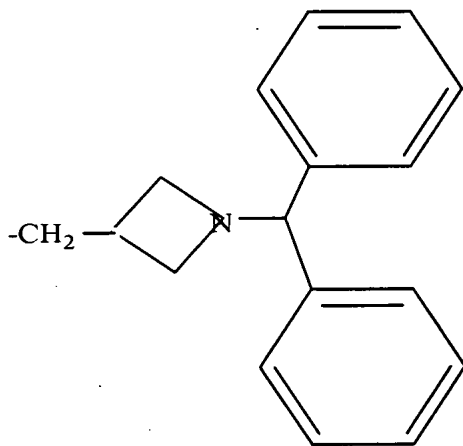
D³
cont

75. A method of inhibiting tumor cell growth according to claim 64, wherein the method is effective for inhibiting tumors selected from the group consisting of gynecological tumors, ovarian carcinomas, testicle tumors, esophagus carcinomas, stomach cancer, rectal carcinomas, pancreas carcinomas, thyroid cancer, adrenal tumors, leukemia, lymphomas, Hodgkin's disease, CNS tumors, soft-tissue sarcomas, bone sarcomas, benign and malignant mesotheliomas, intestine tumors, liver tumors, breast tumors, bronchial and lung carcinomas, melanomas, benign papillomatosis tumors, and combinations thereof.

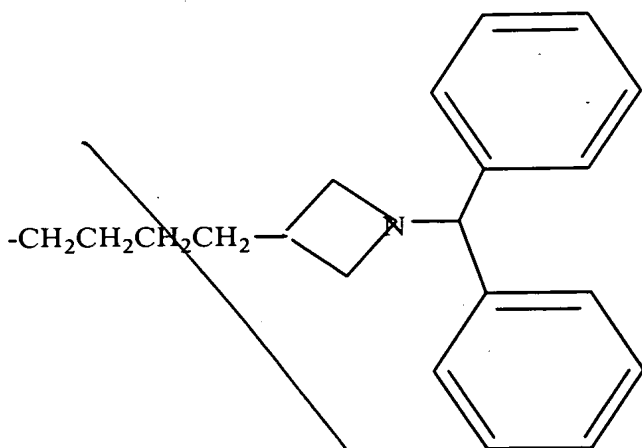
C⁴

76. A method of inhibiting tumor cell growth according to claim 64, wherein the pharmaceutical composition is combined with a compound selected from the group consisting of pharmaceutically acceptable carriers, adjuvants, additives, and mixtures thereof.

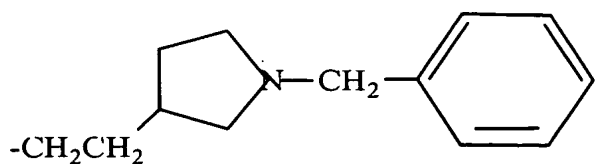
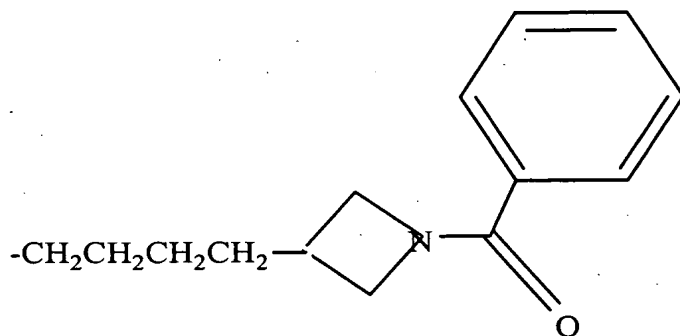
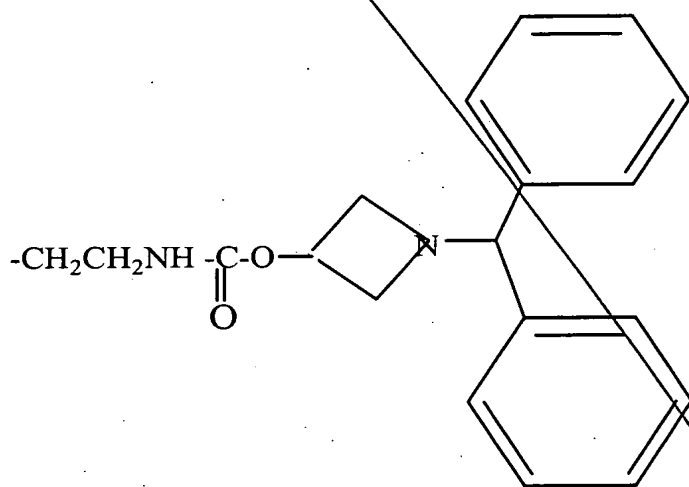
77. A method of inhibiting tumor cell growth according to claim 64, wherein DEG is selected from the group consisting of



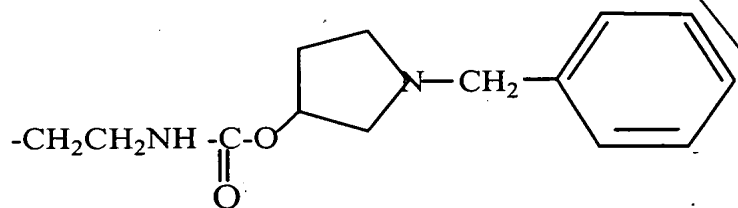
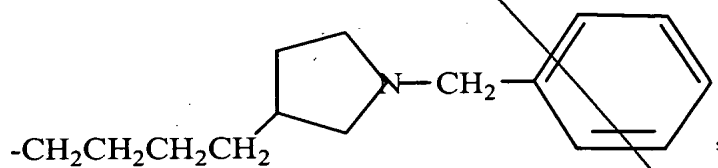
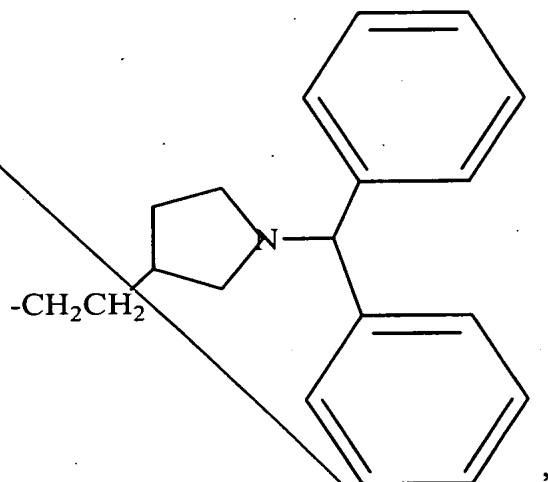
D³
cont



C4

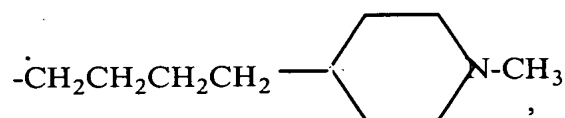
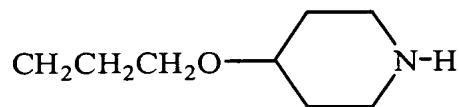
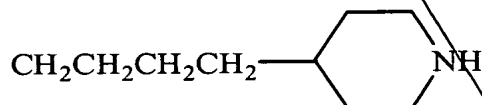
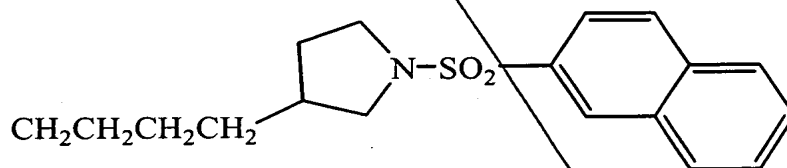
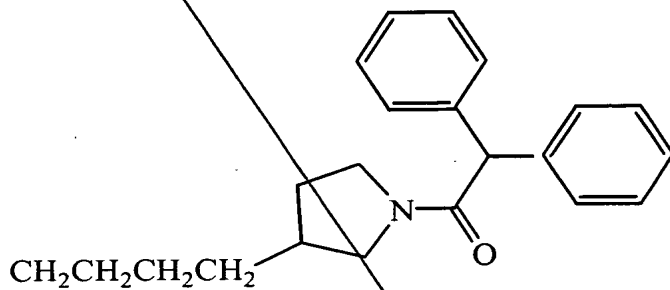
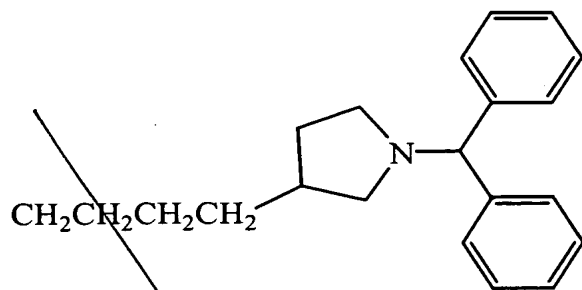


10³
cont

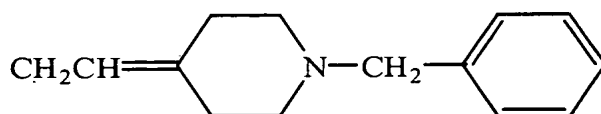
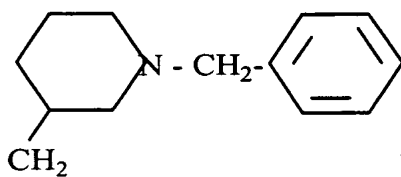
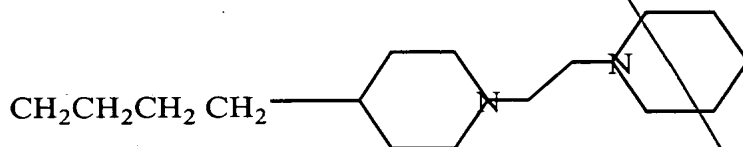
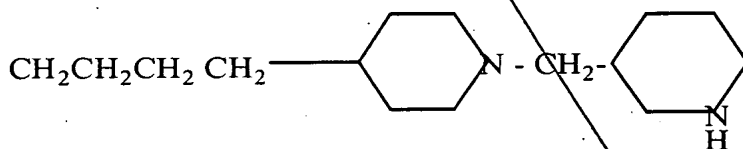
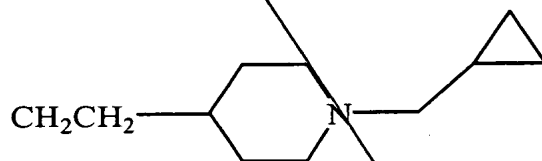
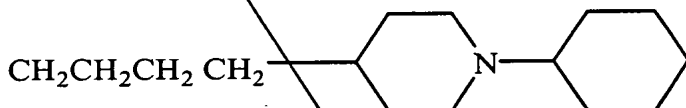
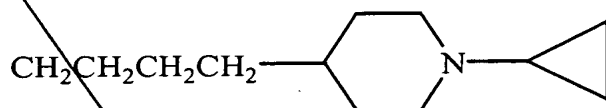
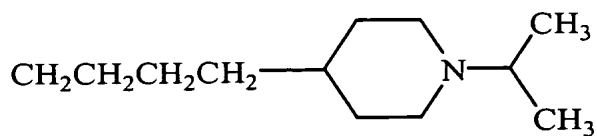


C4

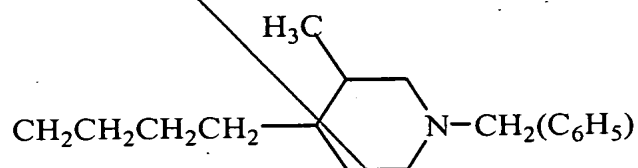
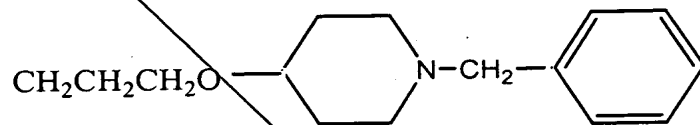
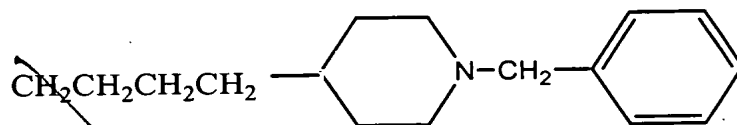
O³
cont



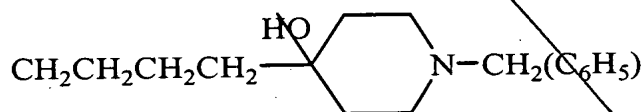
D³
cont



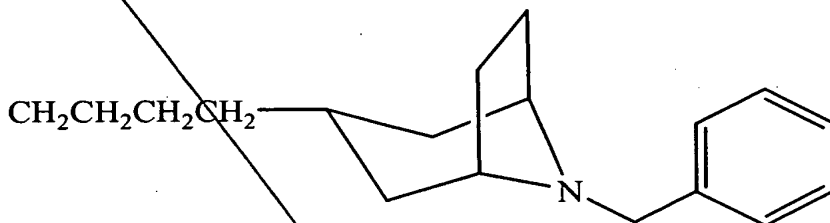
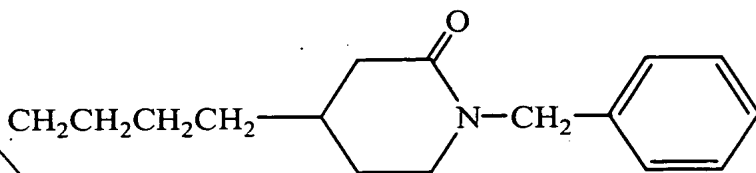
B³
cont



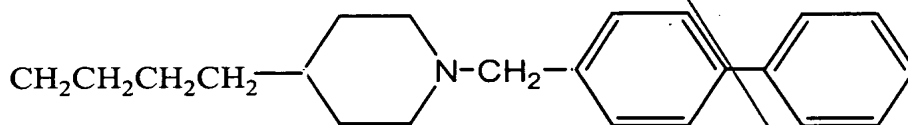
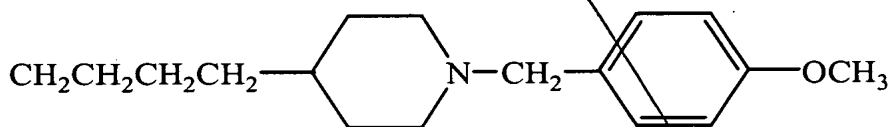
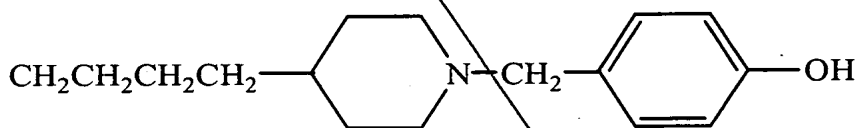
C⁴



D³
cont

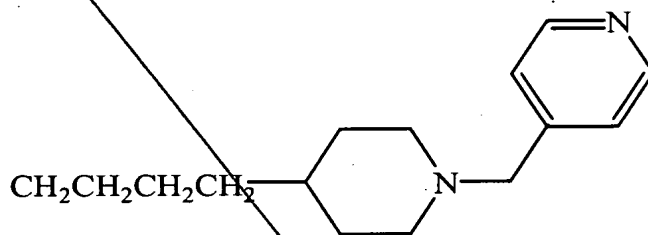
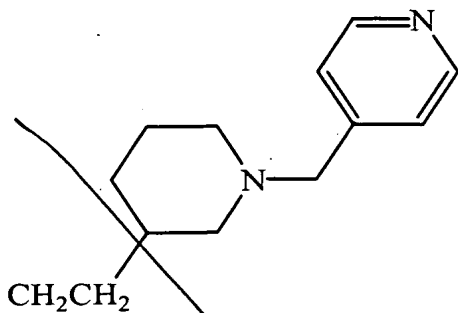


C4

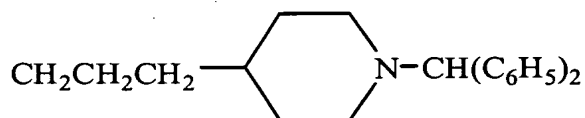
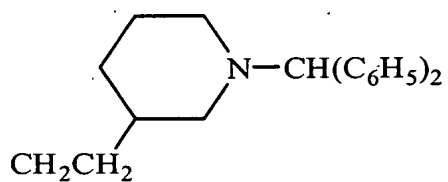
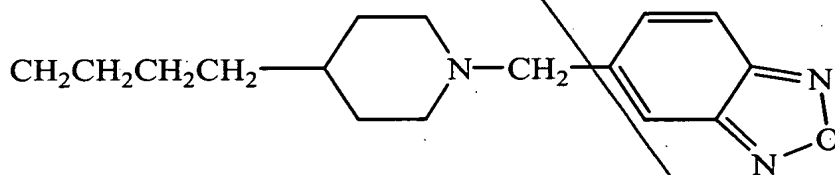


CCCCN1CCCCC1Cc2ccc3ccccc3cc2CCCCN1CCCCC1C2(CCC3=CC=CC=C3)C4=CC=CC=C4

D³
cont

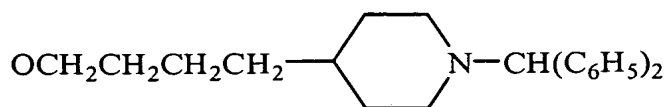
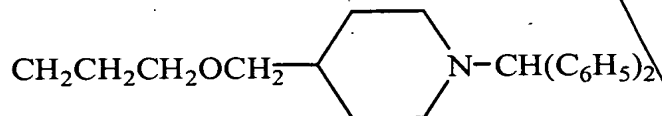
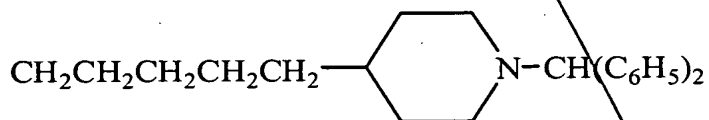
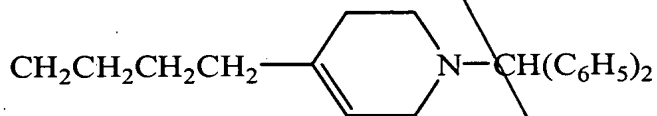
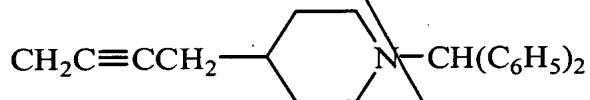
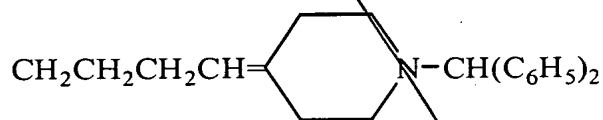
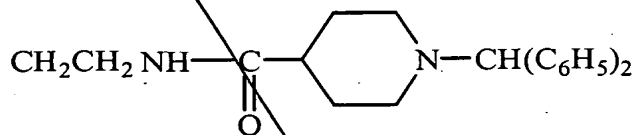
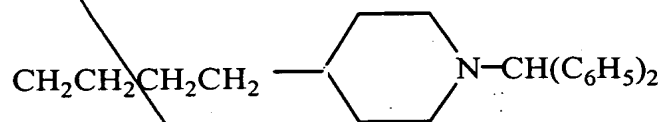
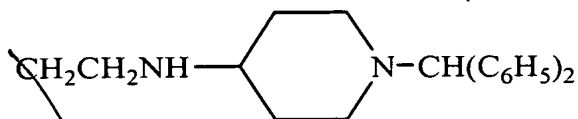


C⁴



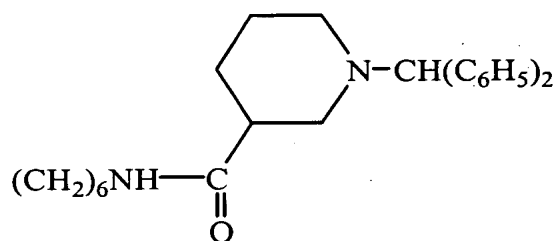
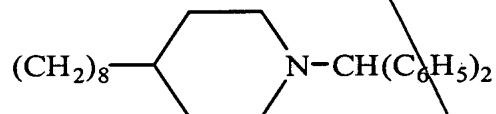
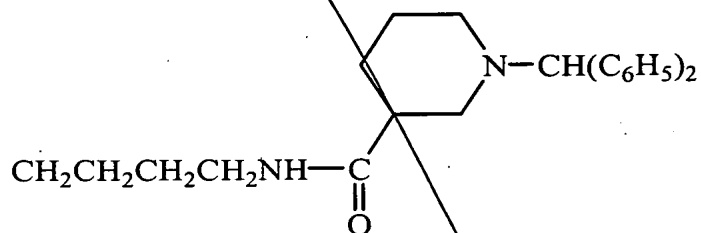
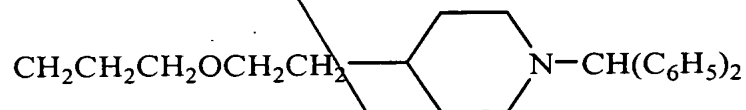
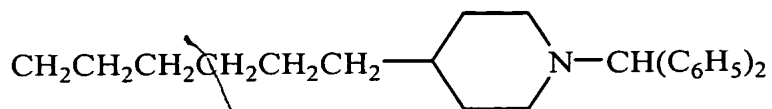
D³
cont

C4

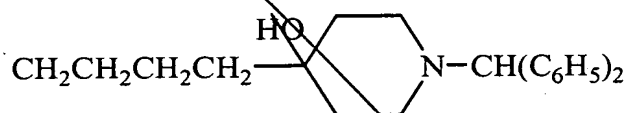
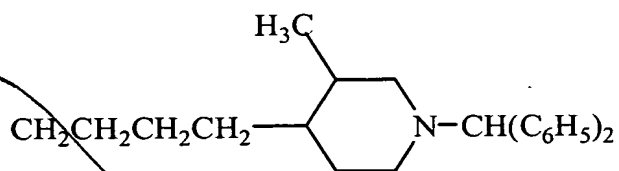


D³
cont

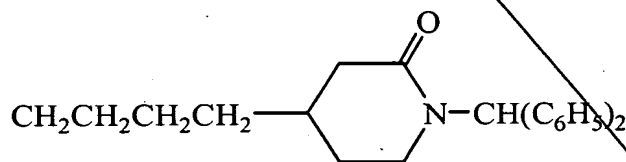
C4



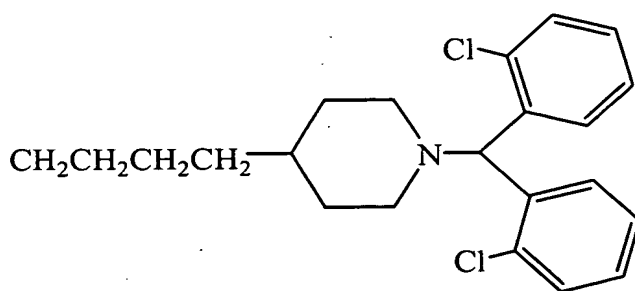
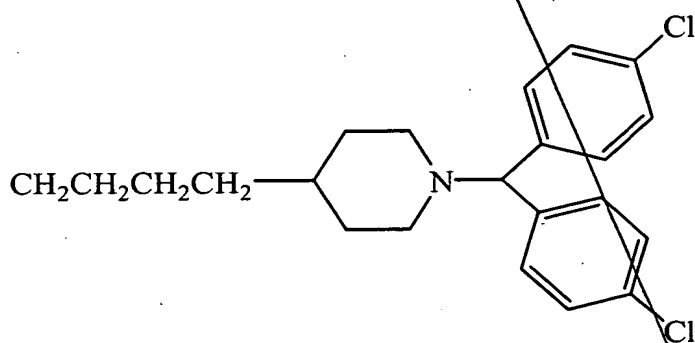
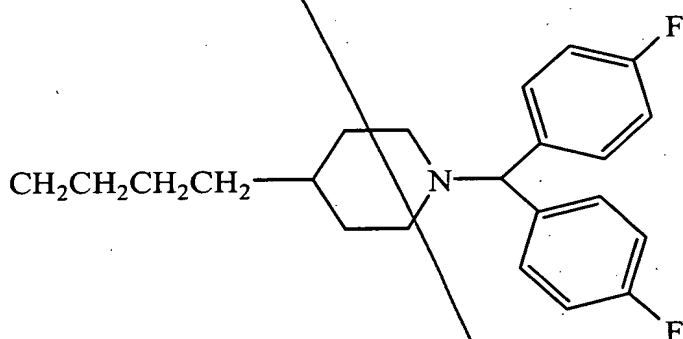
P³
cont



C4

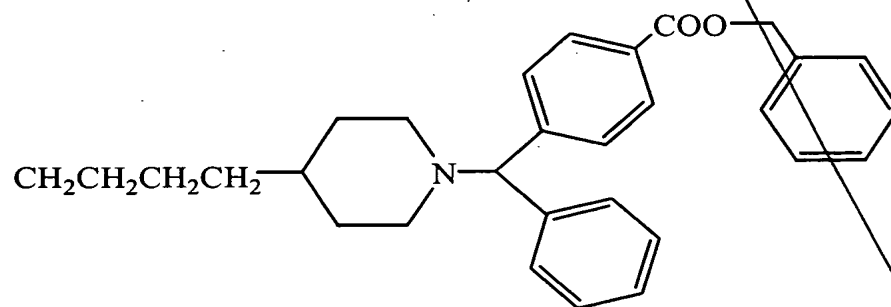
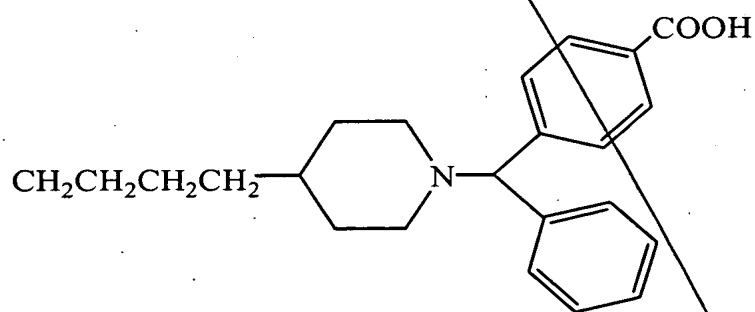
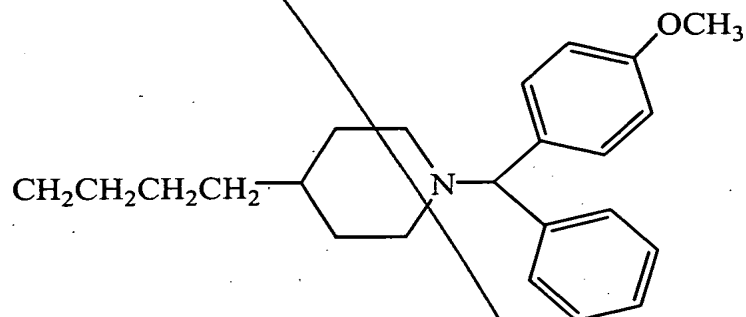
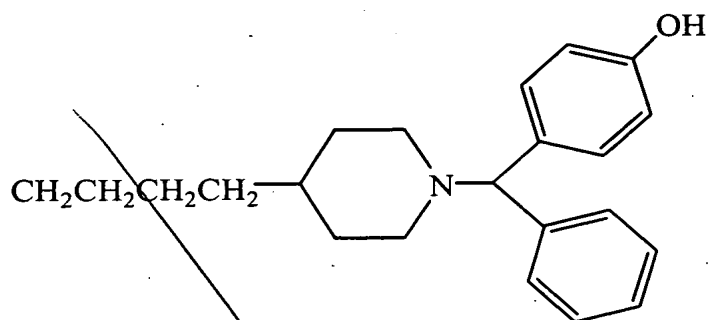


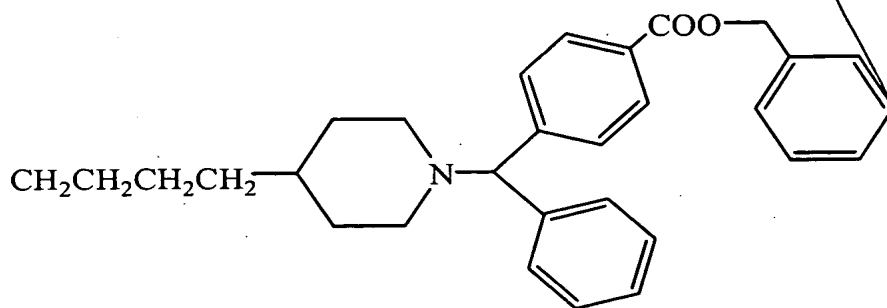
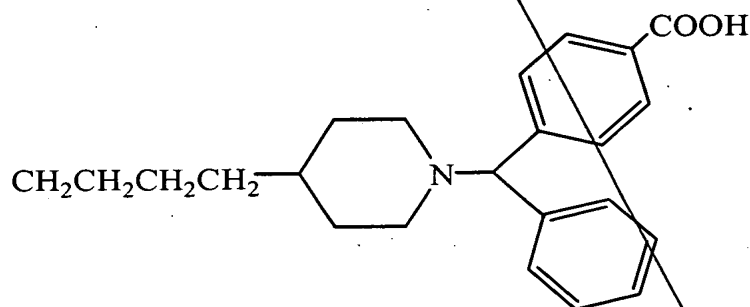
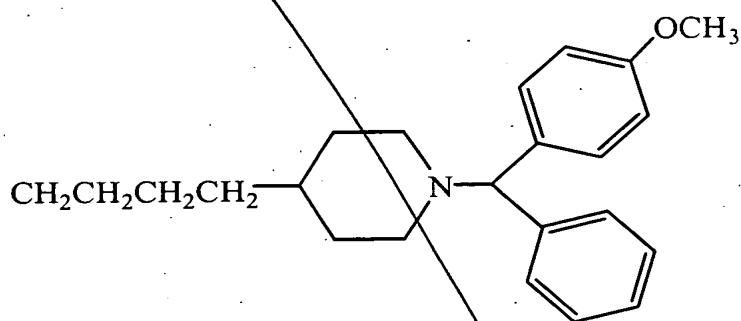
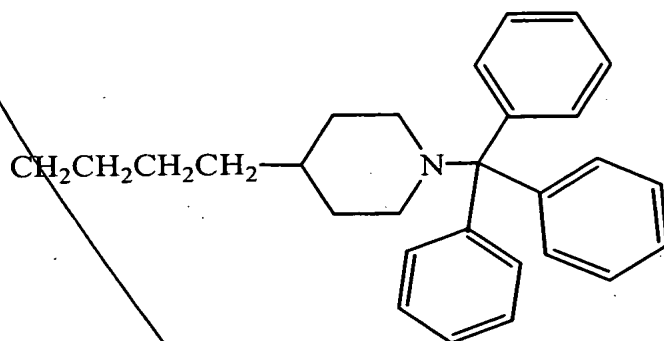
C4



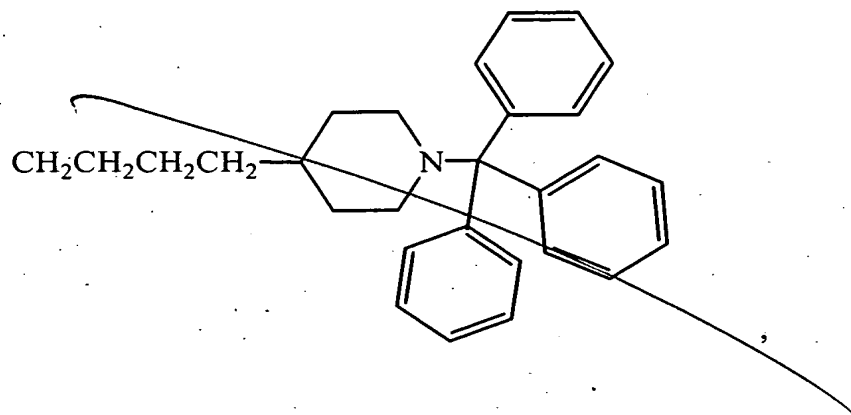
D³
cont

C⁴

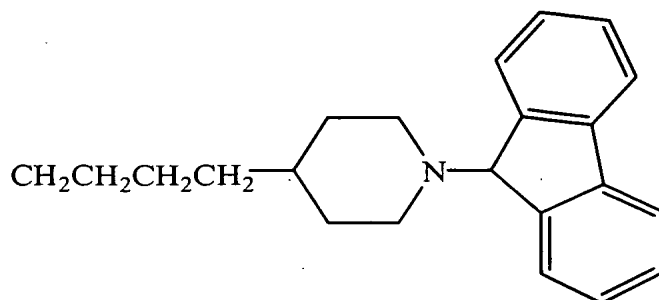
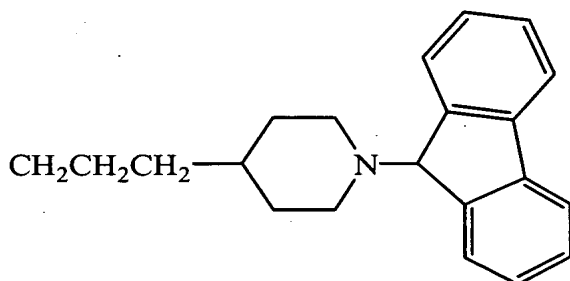
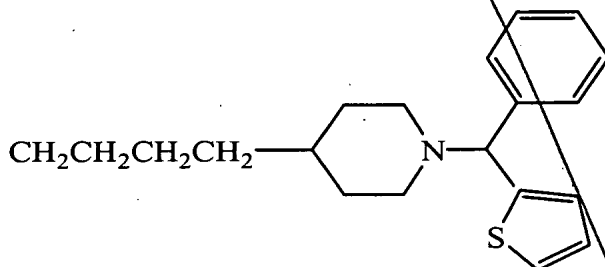
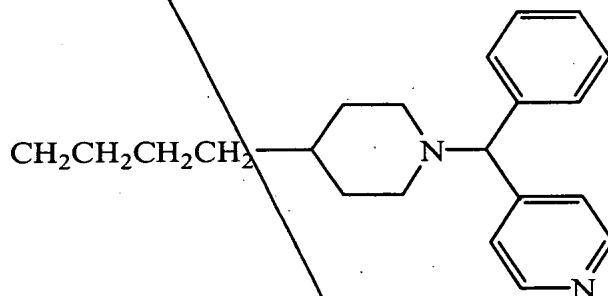
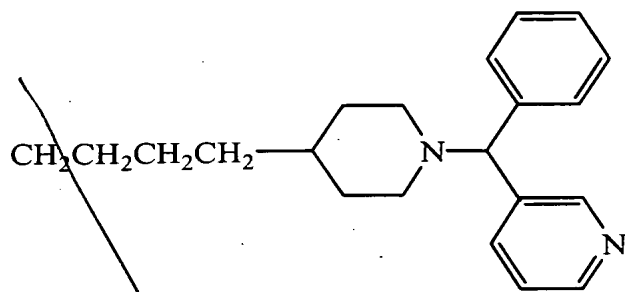




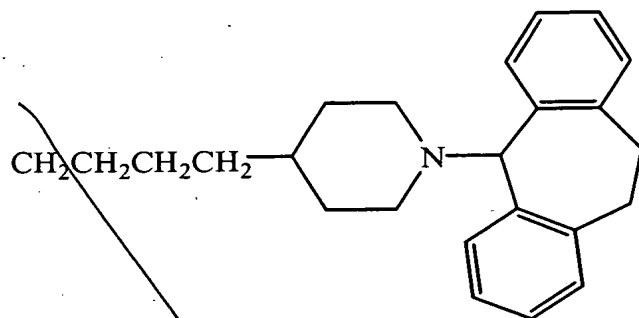
D³
cont



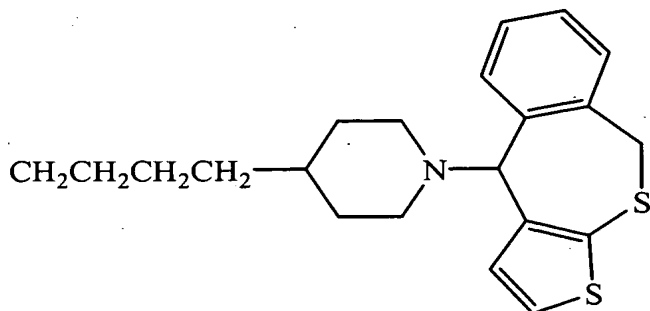
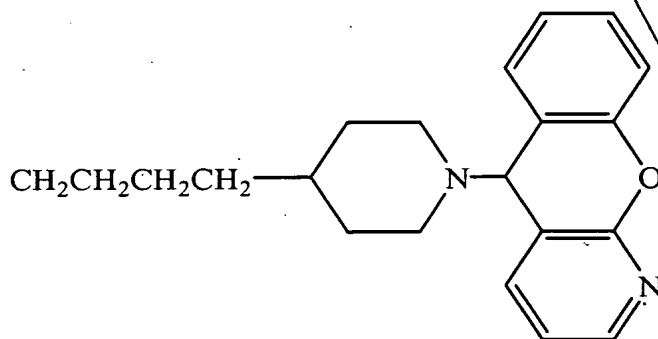
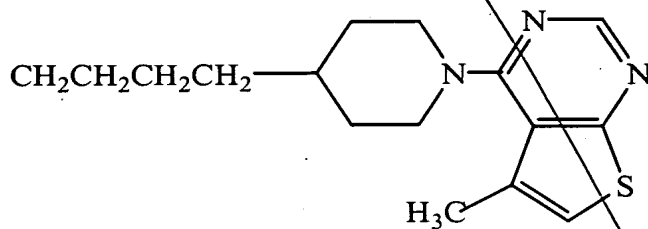
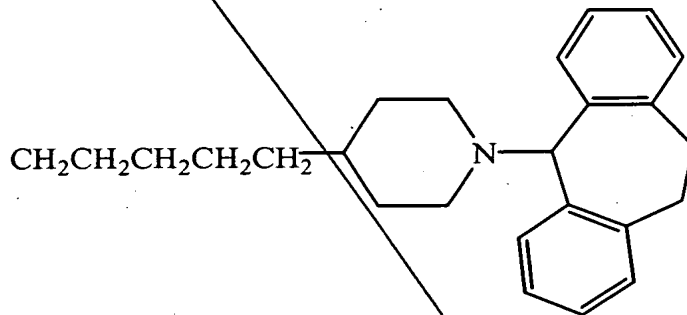
C4



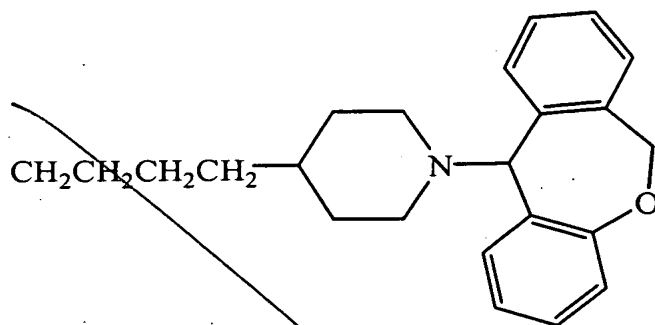
P³
cont



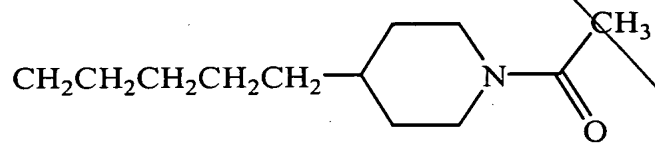
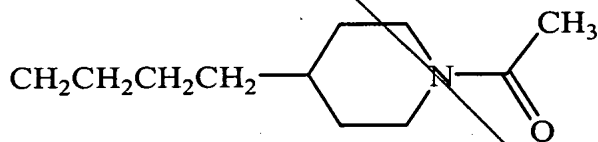
C4



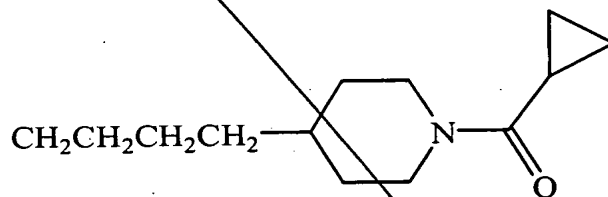
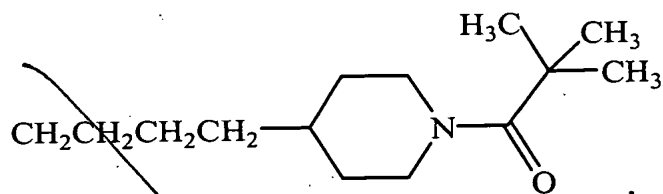
D³
cont



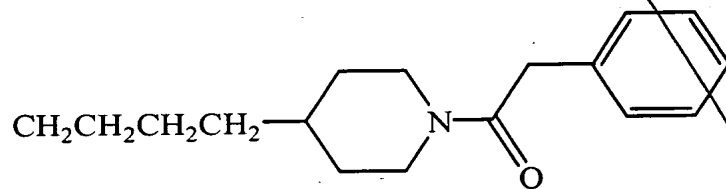
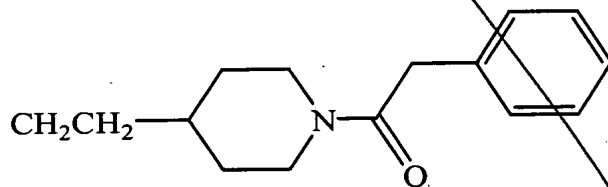
C4



D³
cont

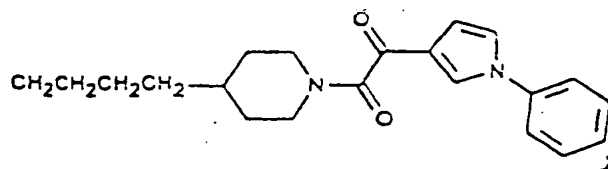
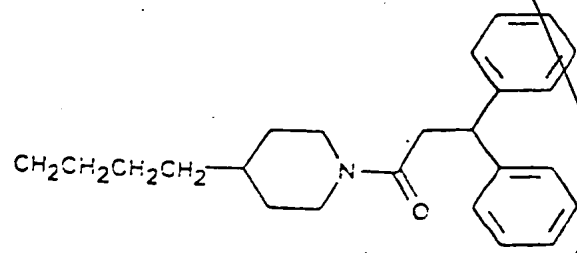
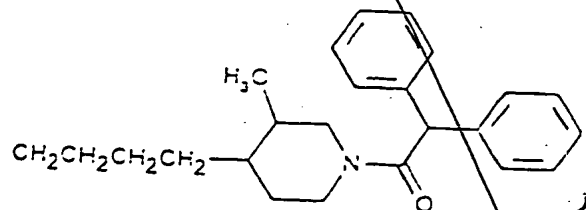
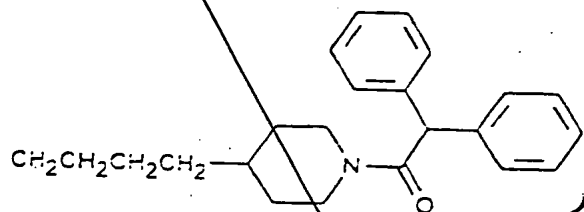
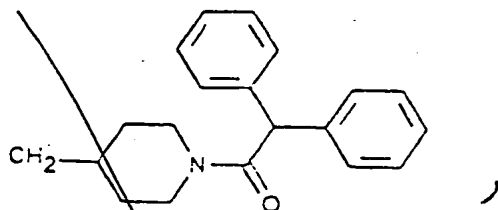


C4



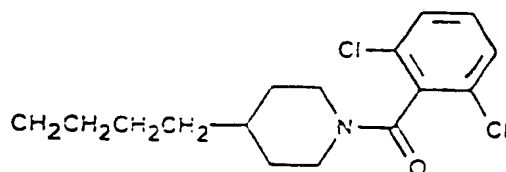
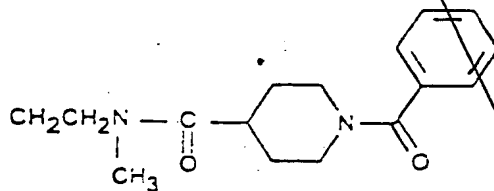
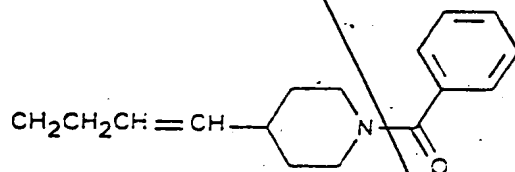
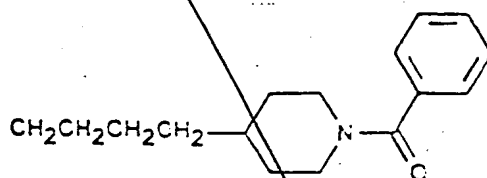
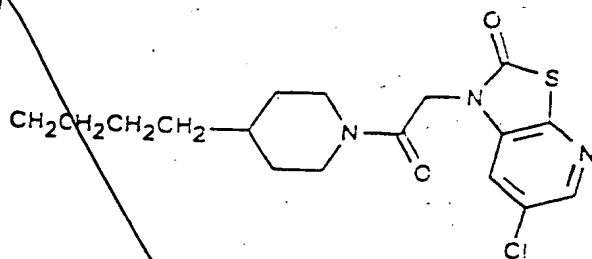
D³
cont

C⁴



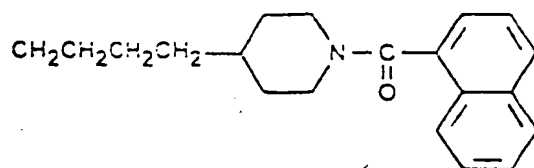
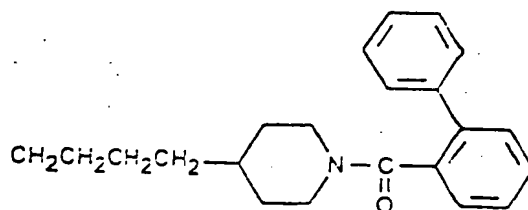
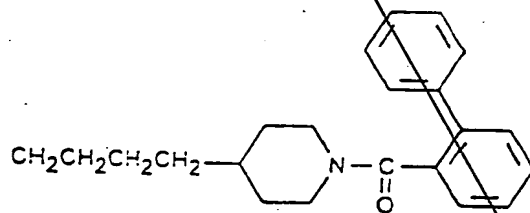
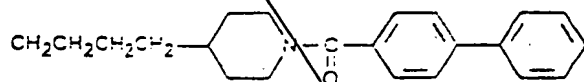
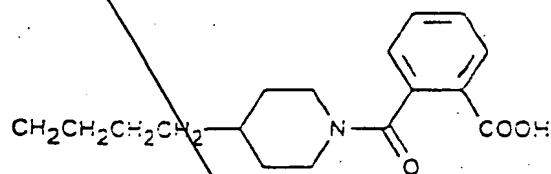
D³
cont

C4



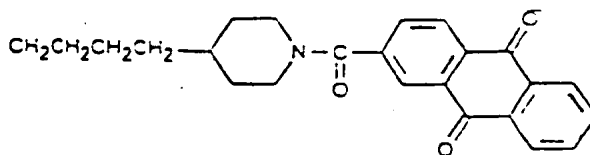
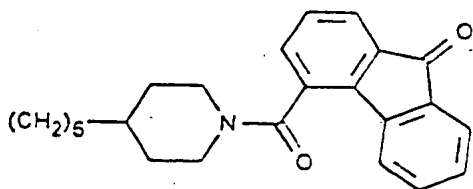
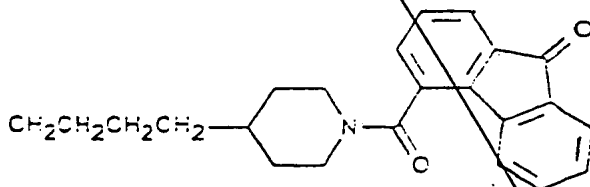
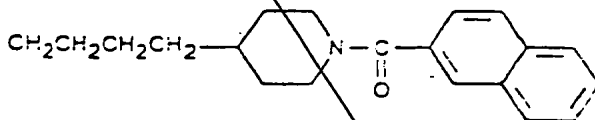
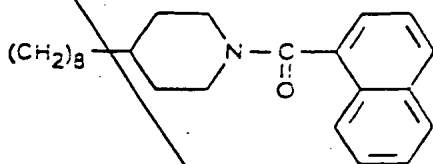
D³
cont

C4



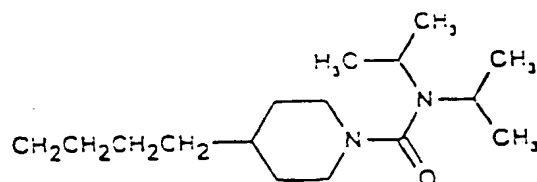
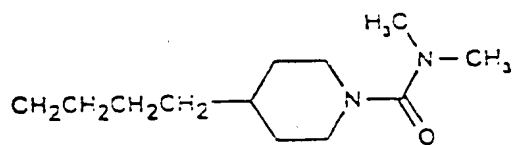
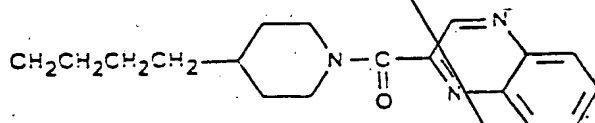
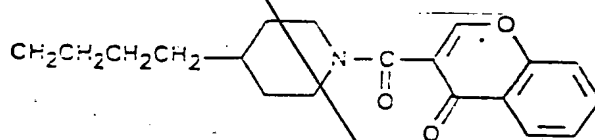
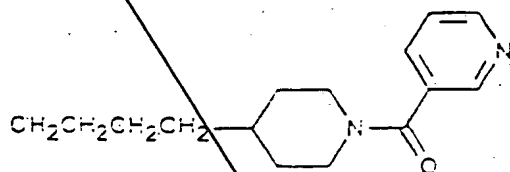
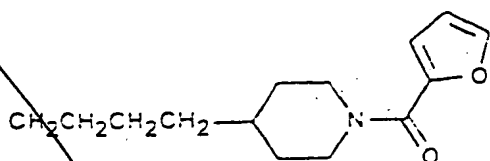
O3
cont

C4



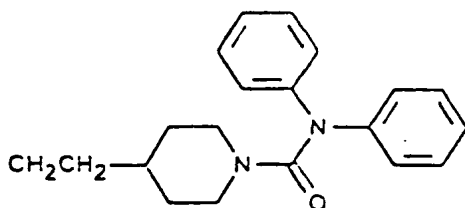
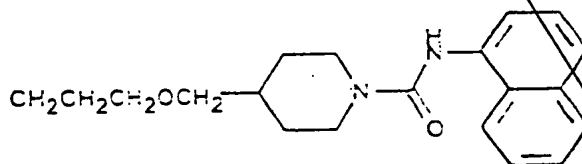
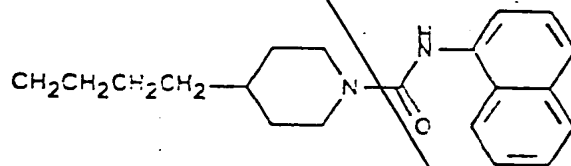
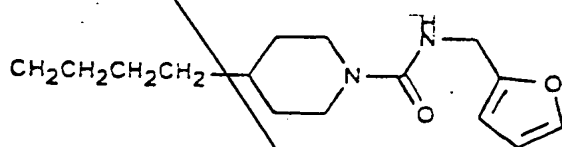
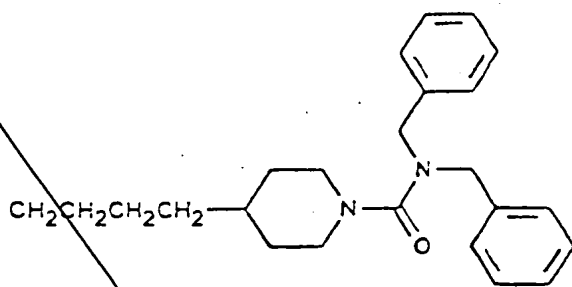
B3
cont

C4



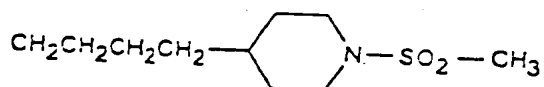
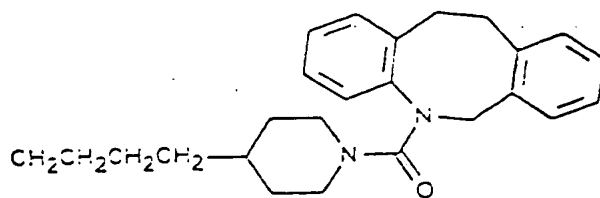
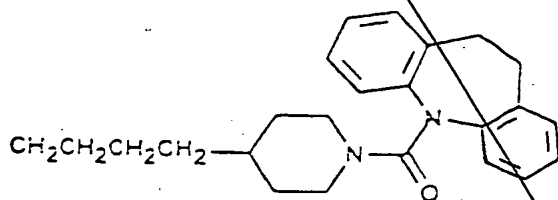
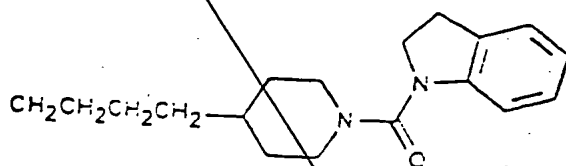
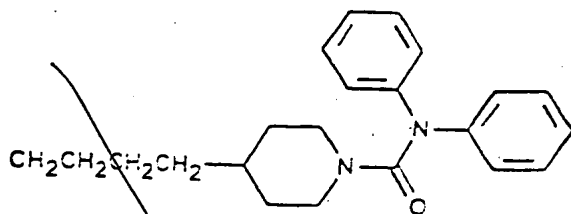
D³
cont

C⁴



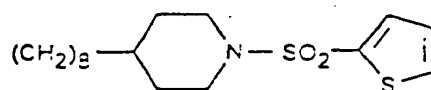
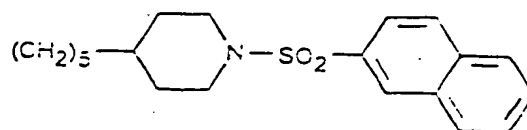
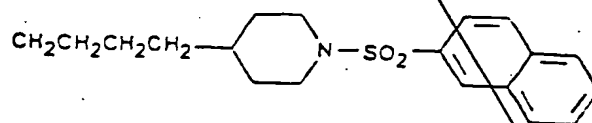
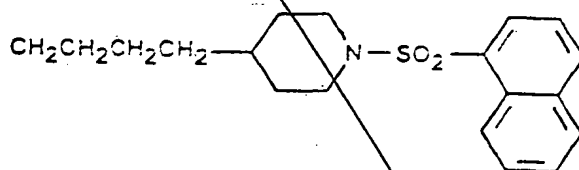
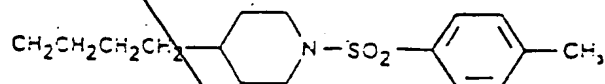
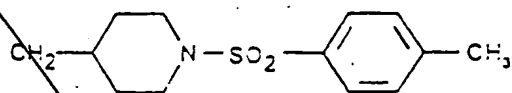
P³
cont

C4



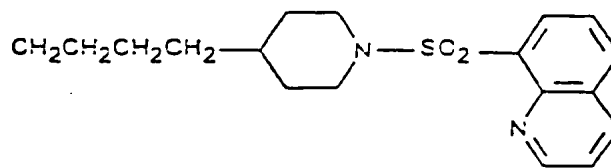
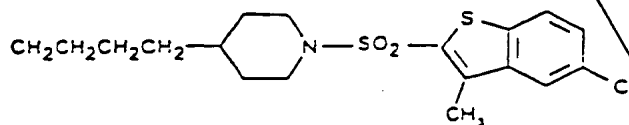
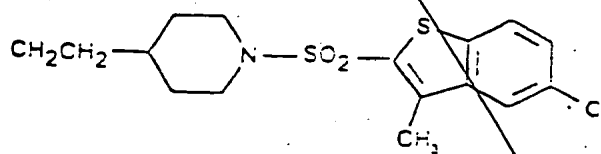
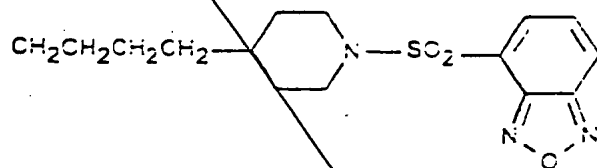
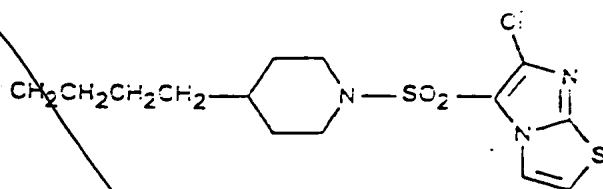
D³
cont

C⁴

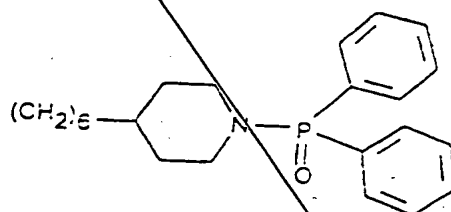
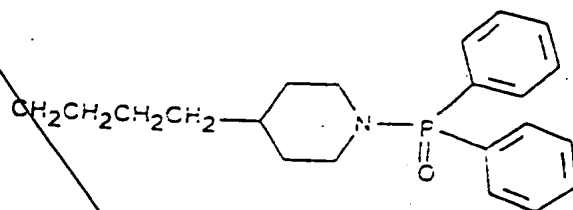


D³
cont

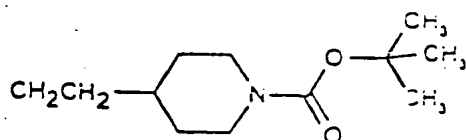
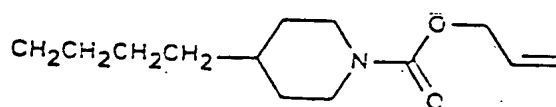
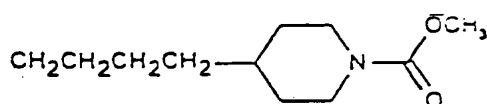
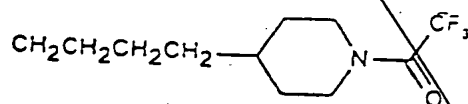
C4



D3
cont

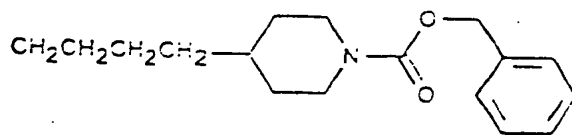
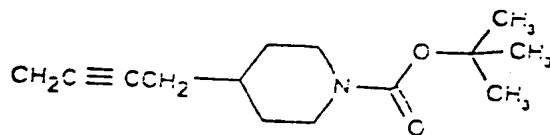
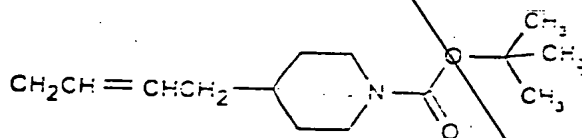
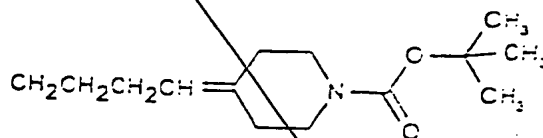
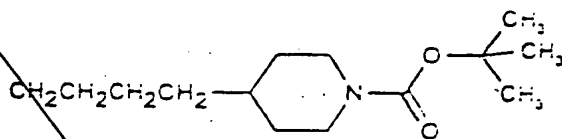


C4

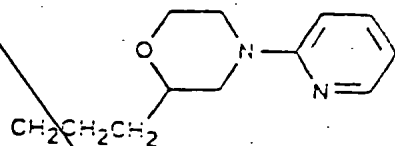
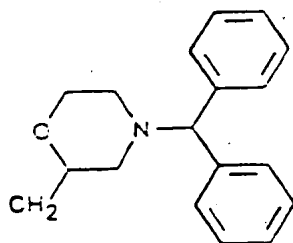


D³
cont

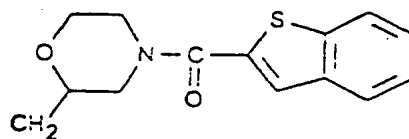
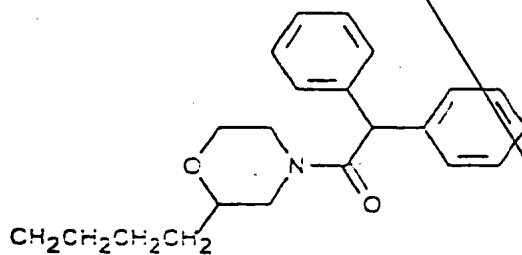
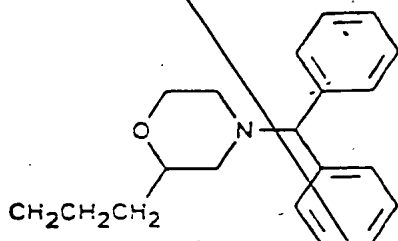
C4



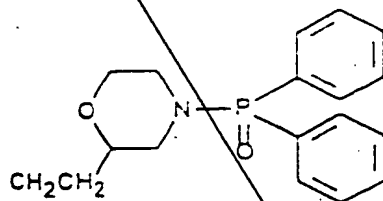
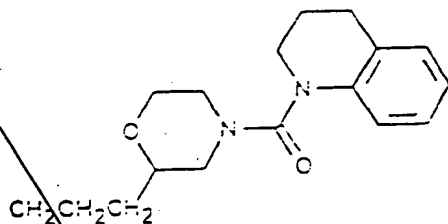
O³
cont



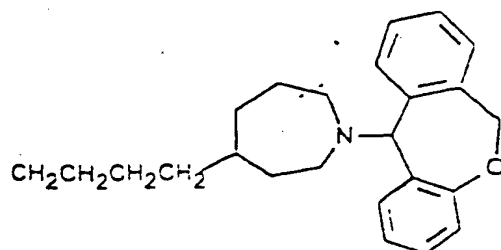
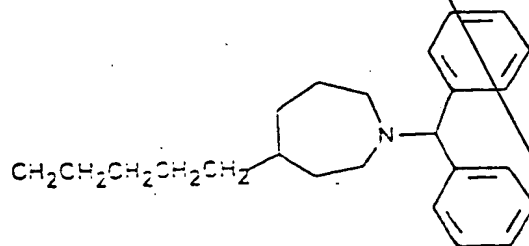
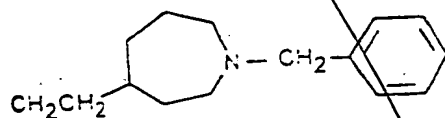
C4



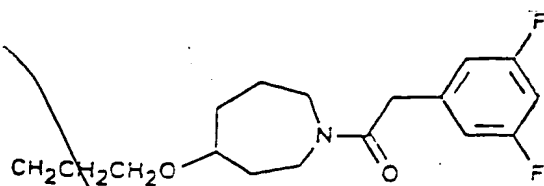
P³
cont



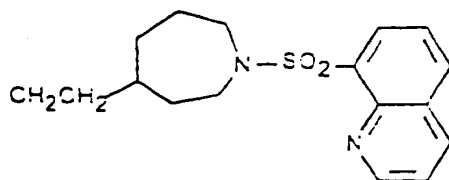
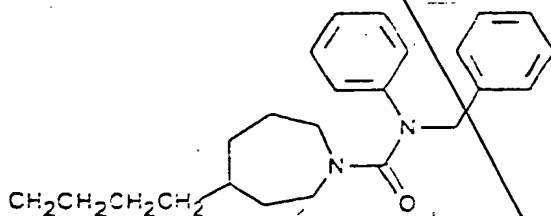
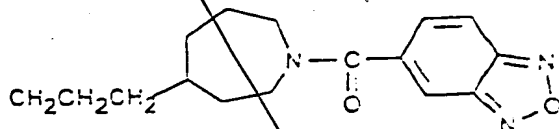
C4



B³
cont

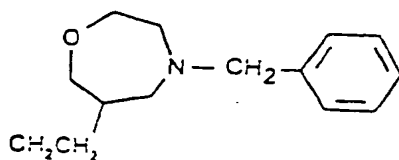
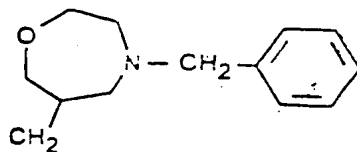
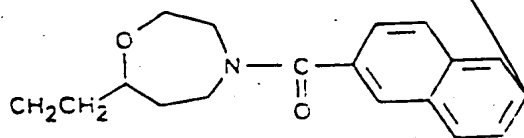
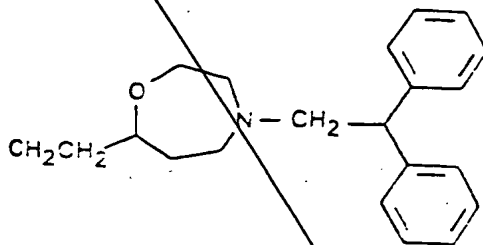
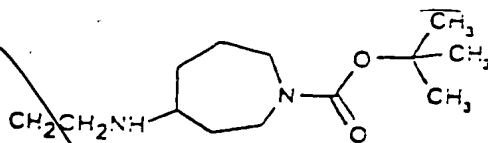


C4



D³
cont

C4



78.. A method of suppressing autoimmune disease according to claim 65, wherein the composition is administered by a method selected from the group consisting of subcutaneously, intramuscularly, intravenously, intracutaneous, orally, sublingually, transdermally, topically, and combinations thereof.

79. A method of suppressing autoimmune disease according to claim 65, wherein the composition is administered in combination with other immunosuppressive agents.

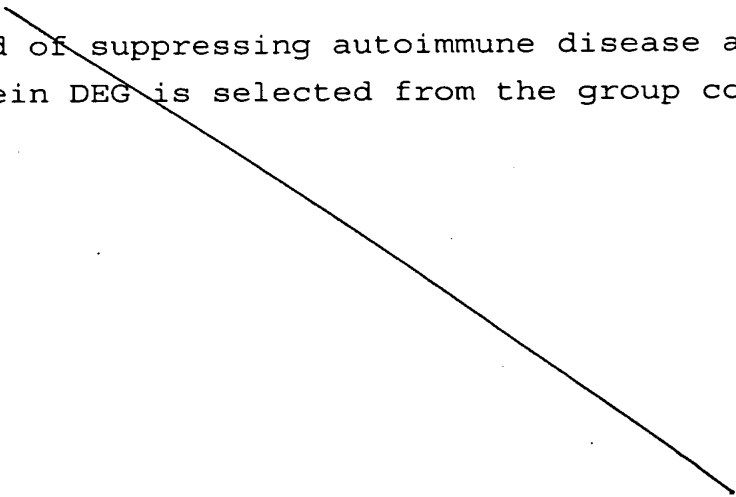
C4
80. A method of suppressing autoimmune disease according to claim 65, wherein the other immunosuppressive agents are selected from the group consisting of cyclosporin A, tacrolimus, rapamycin, and mixtures thereof;

antimetabolites selected from the group consisting of methotrexate, azothiaprime, and mixtures thereof; and glucocorticoids.

81. A method of suppressing autoimmune disease according to claim 65, wherein the pharmaceutical composition is combined with a compound selected from the group consisting of pharmaceutically acceptable carriers, adjuvants, additives, and mixtures thereof.

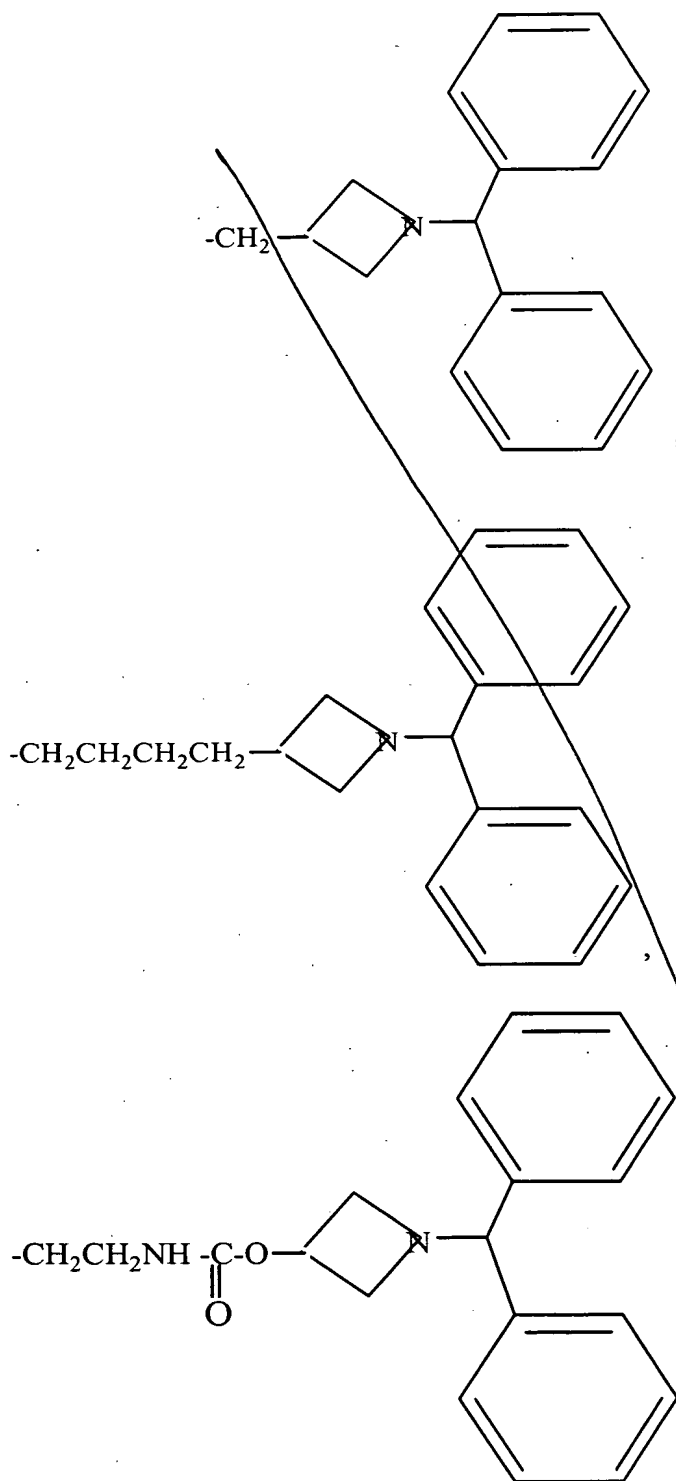
82. A method of suppressing autoimmune disease according to claim 65, wherein DEG is selected from the group consisting of

push
D4



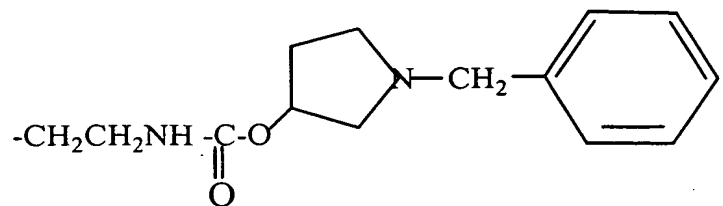
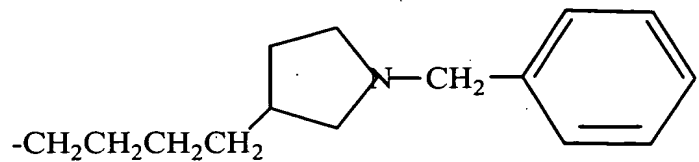
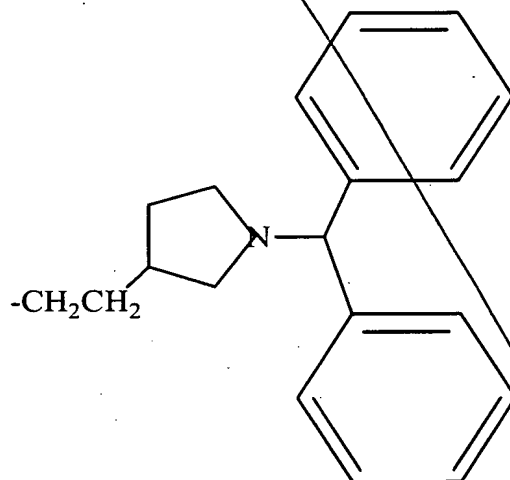
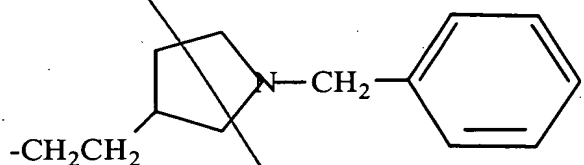
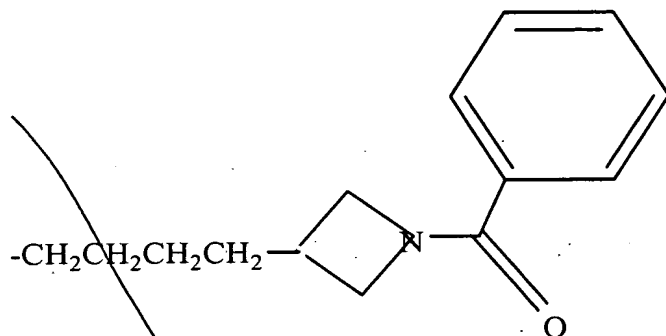
D4
cont

C4



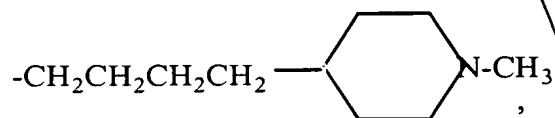
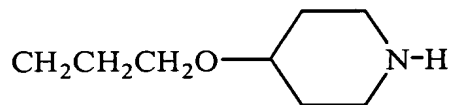
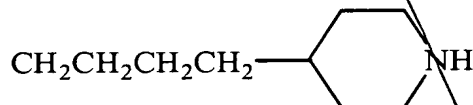
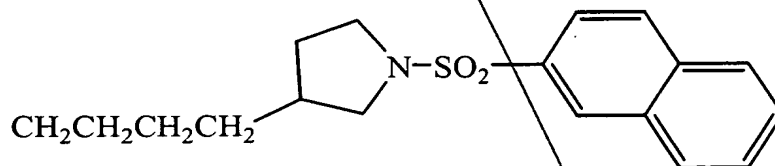
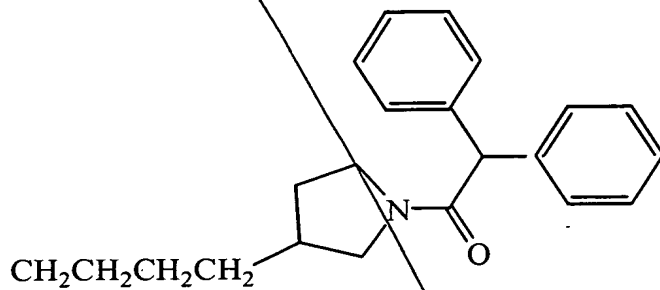
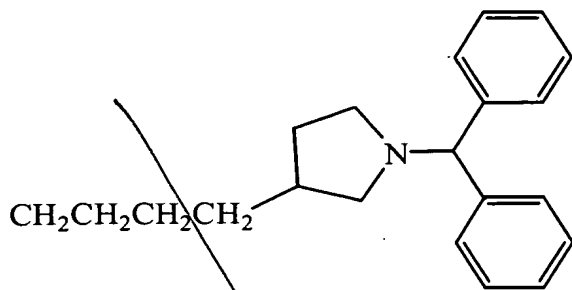
94
Cont

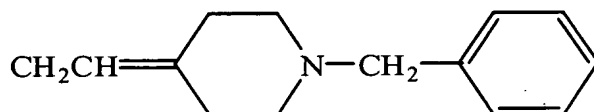
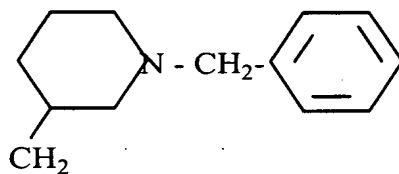
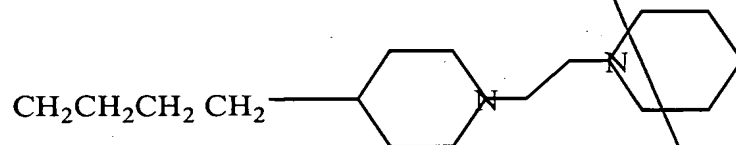
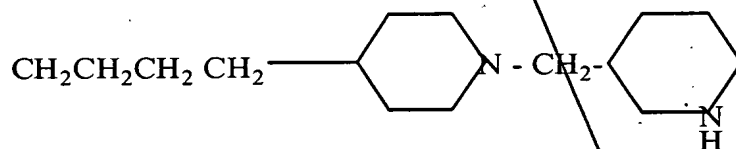
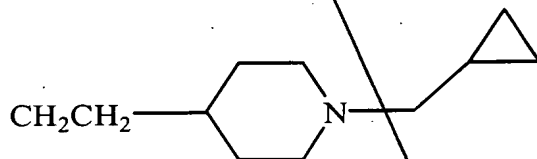
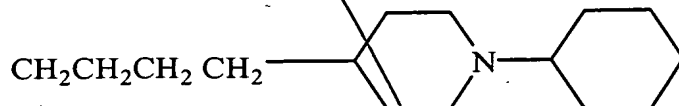
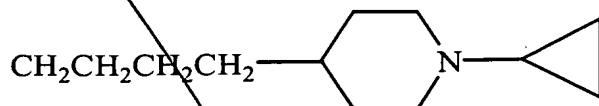
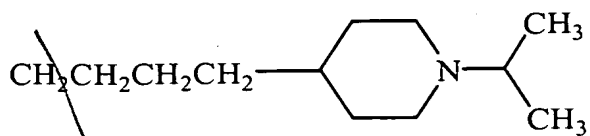
C4



O4
cont

C4

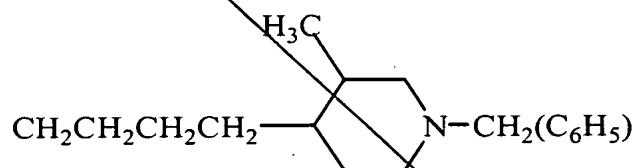
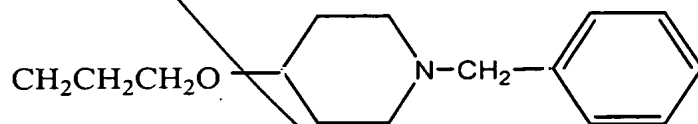
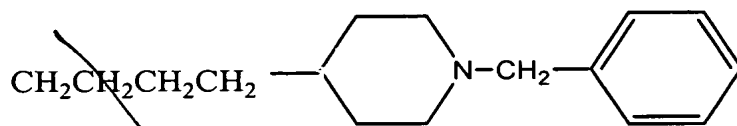




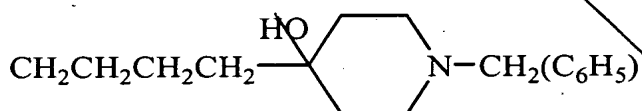
94
cont

C4

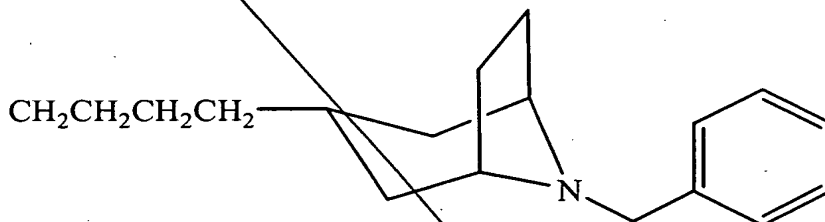
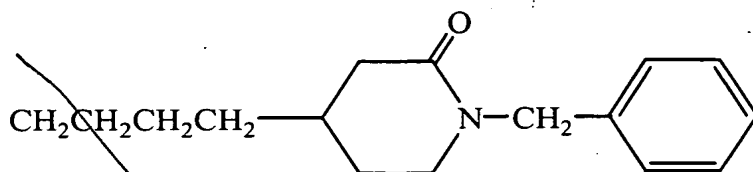
104
cont



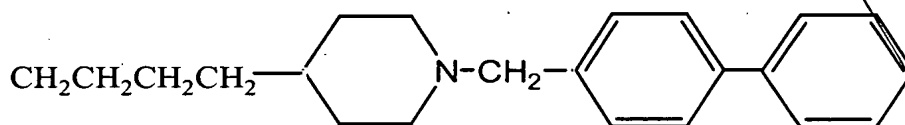
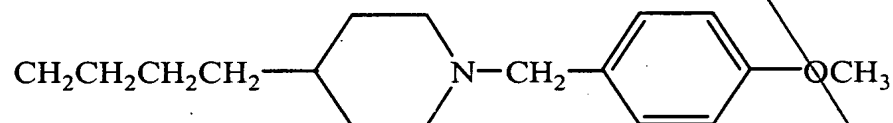
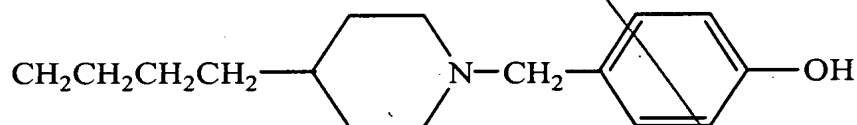
C4



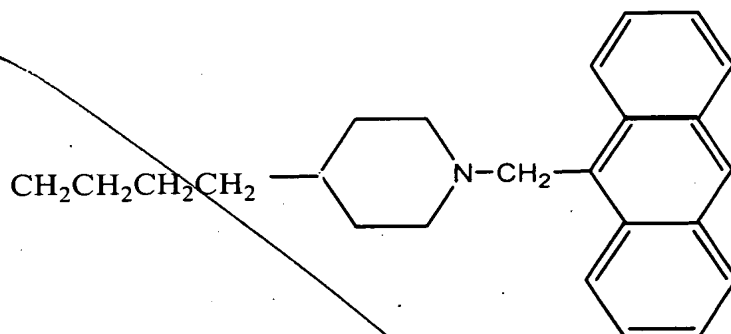
04
cont



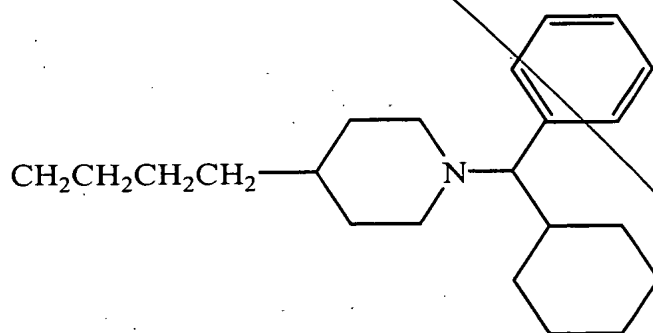
C4



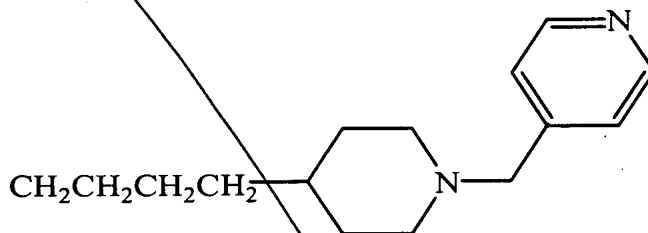
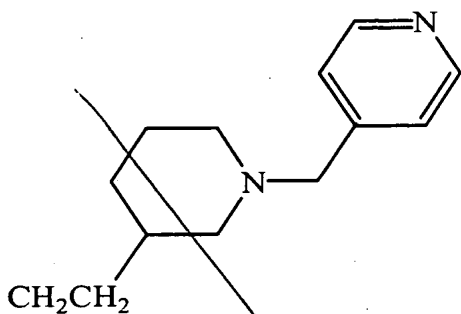
DY
cont



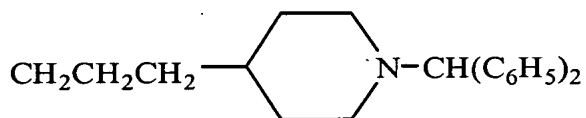
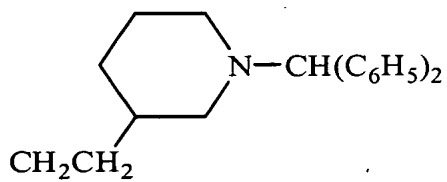
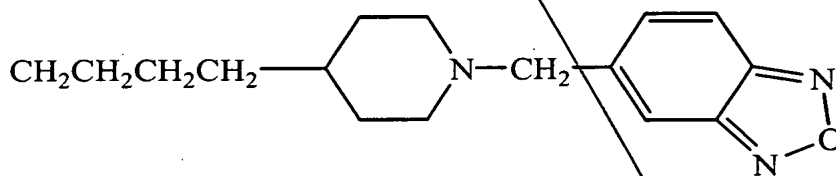
C4



04
cont

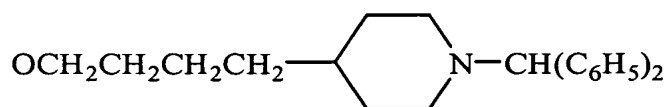
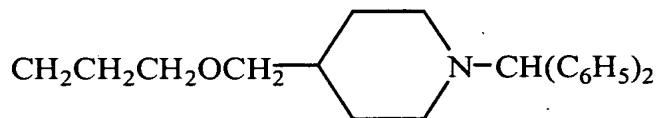
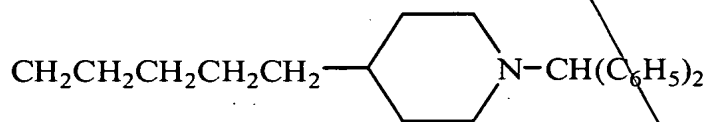
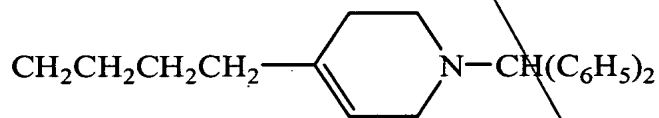
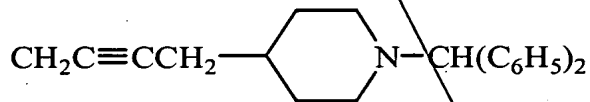
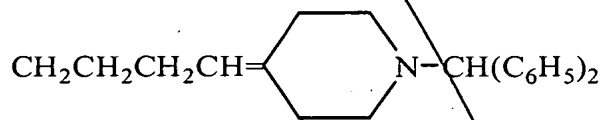
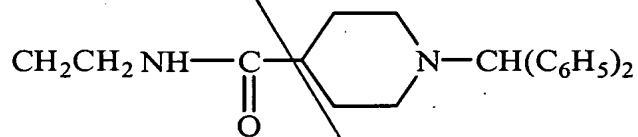
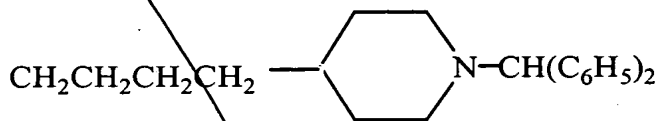
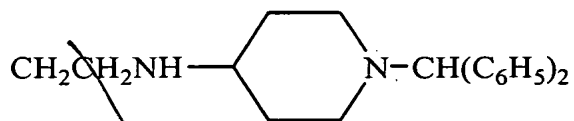


C4



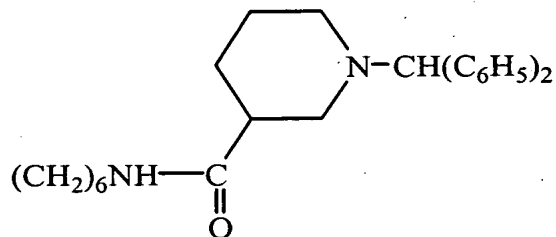
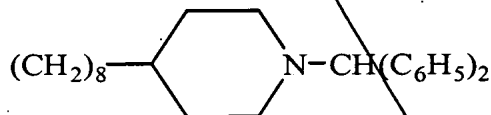
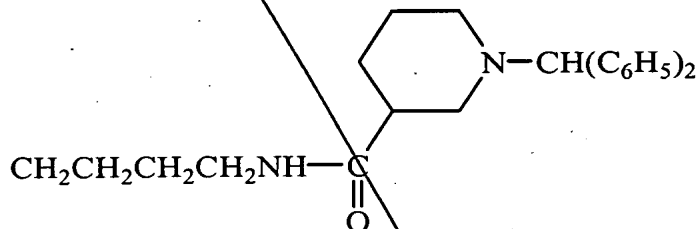
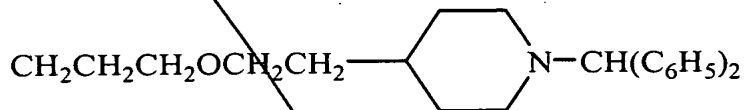
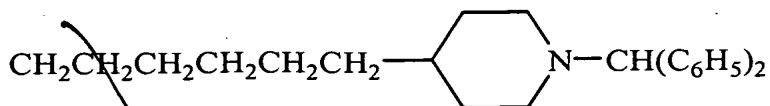
84
cont

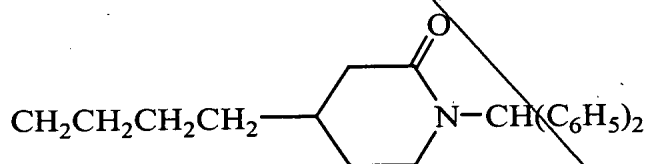
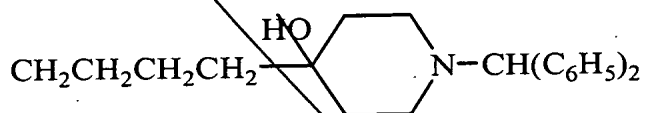
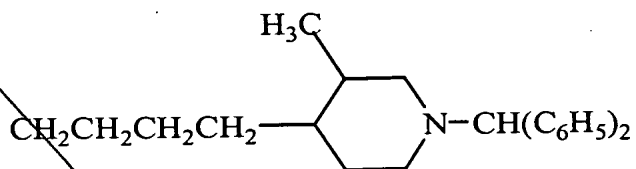
C4



94
cont

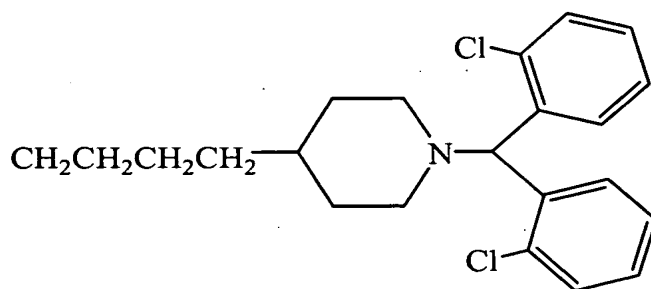
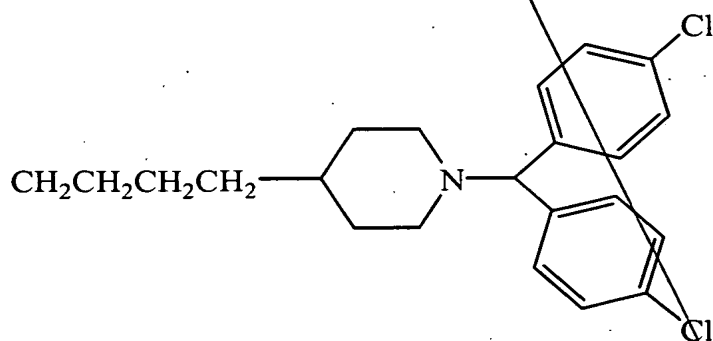
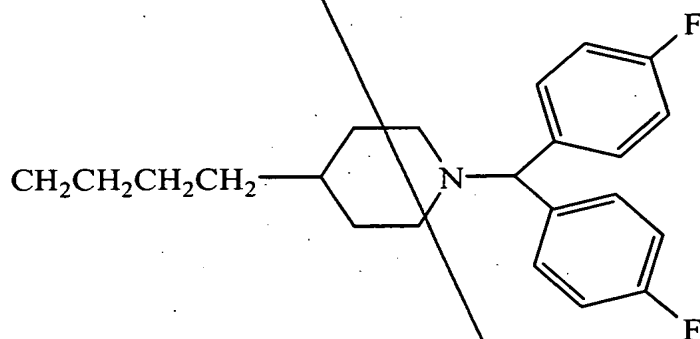
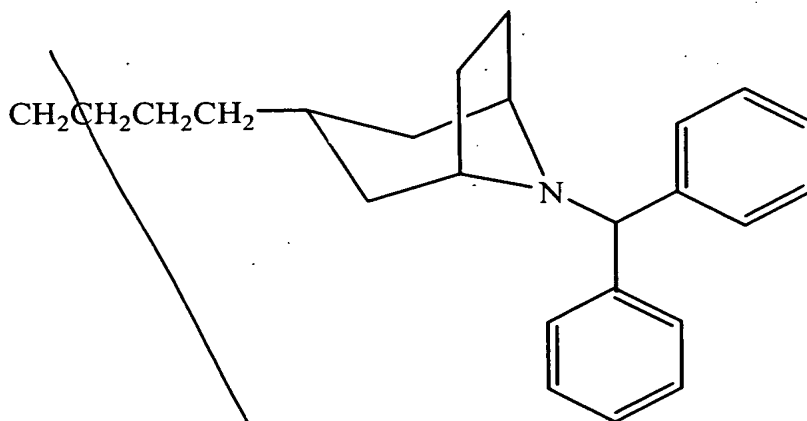
C4





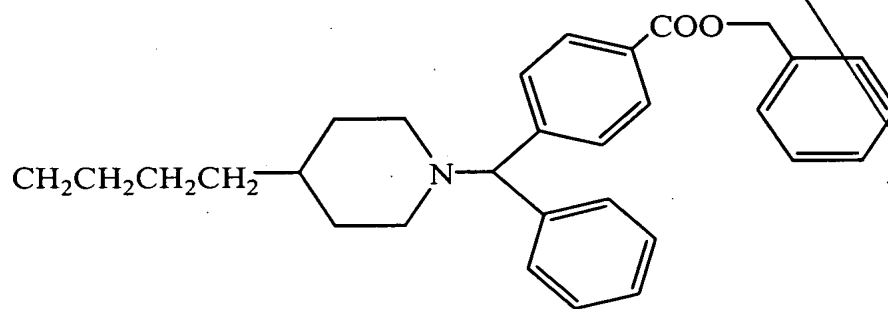
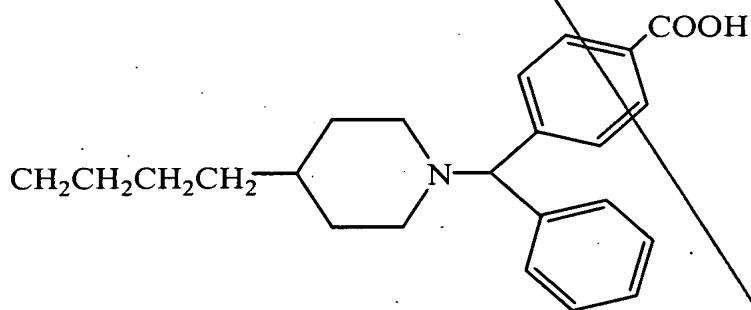
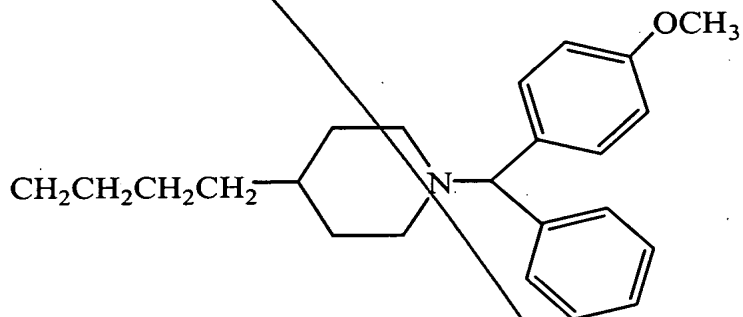
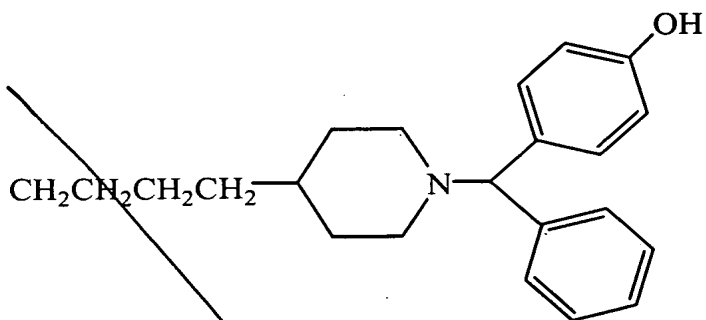
04
cont

C4

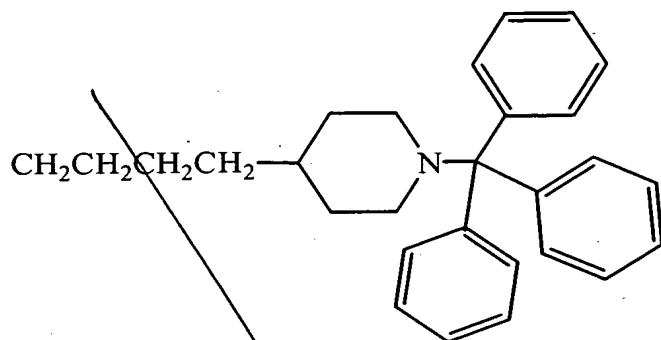


O4
cont

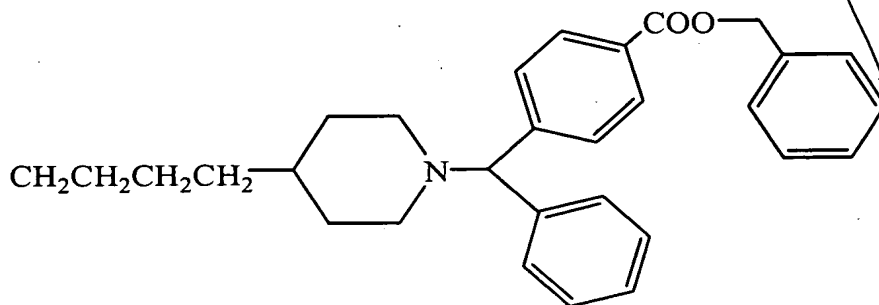
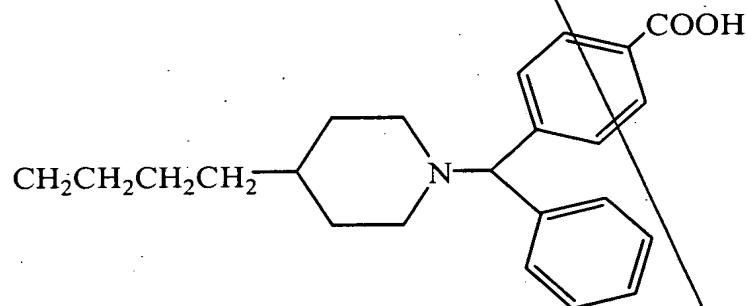
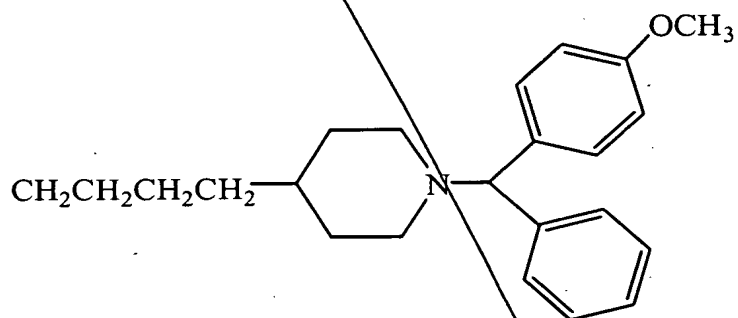
C4



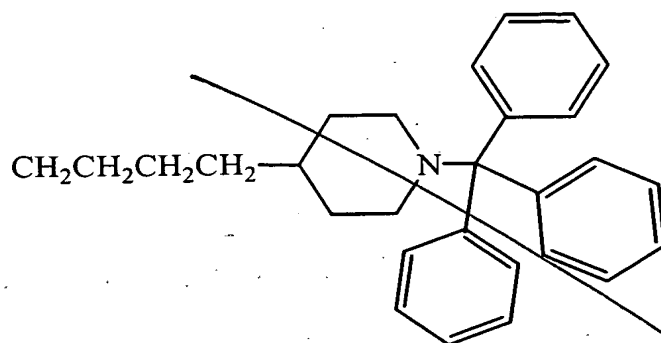
194
cont



C4



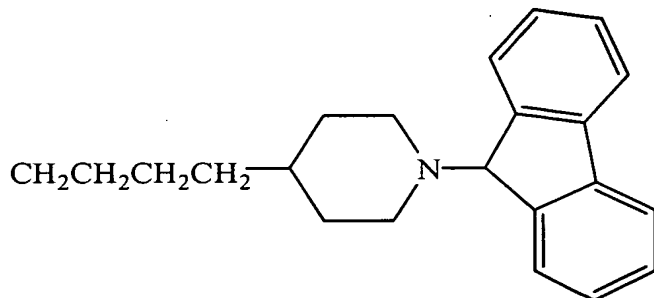
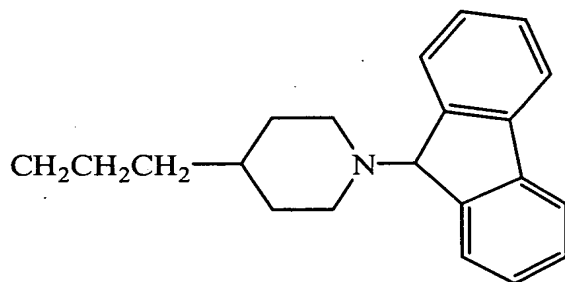
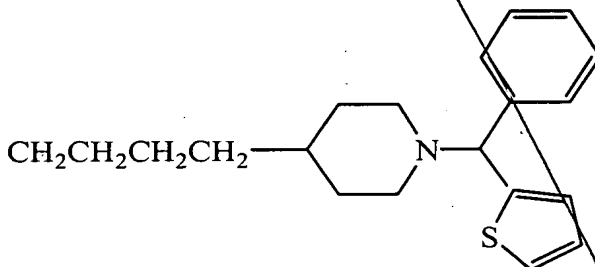
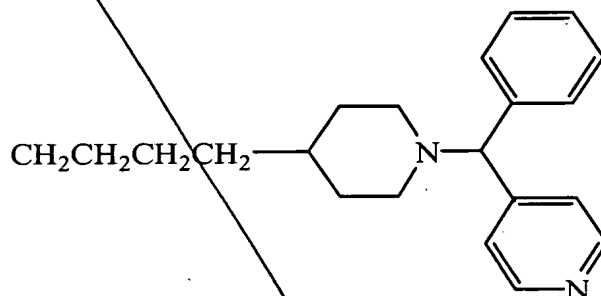
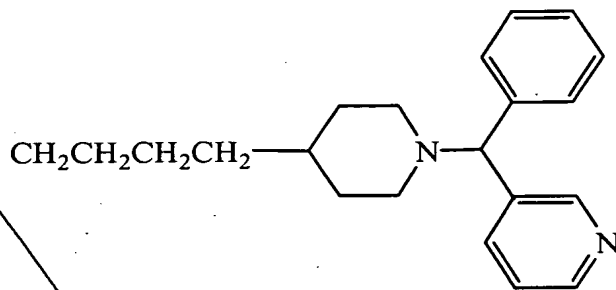
D4
cont



C4

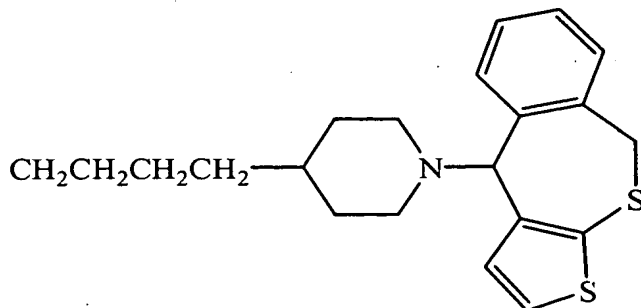
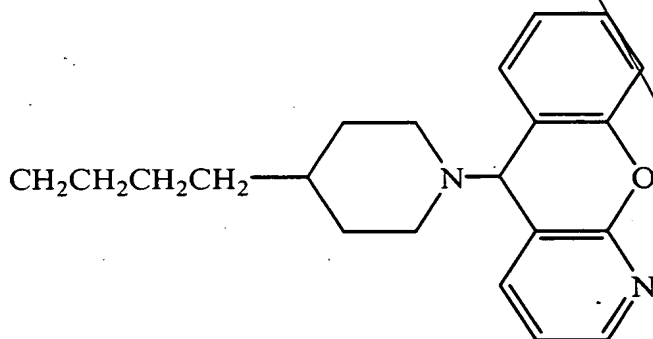
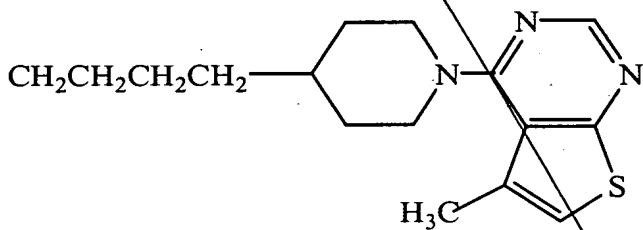
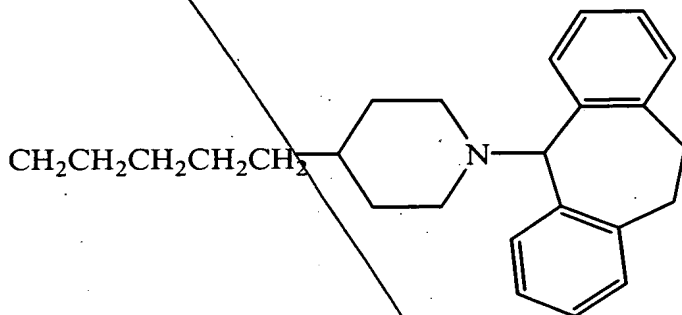
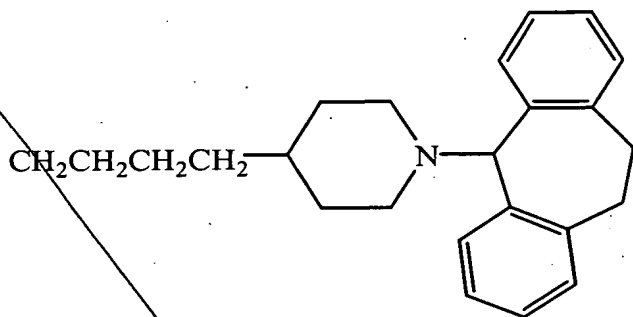
Pf
cont

C4



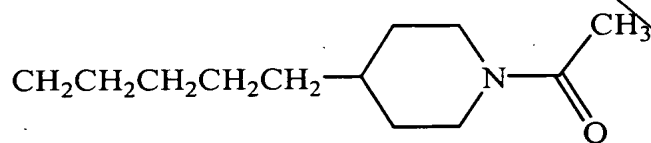
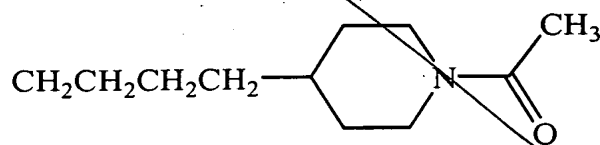
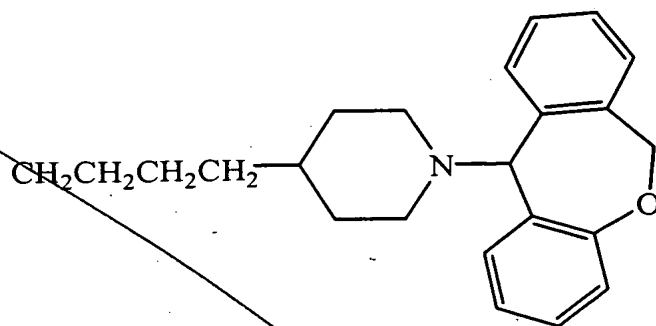
94
cont

C4



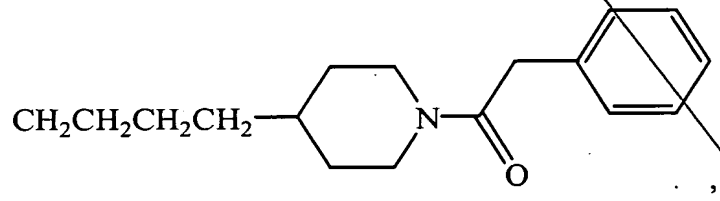
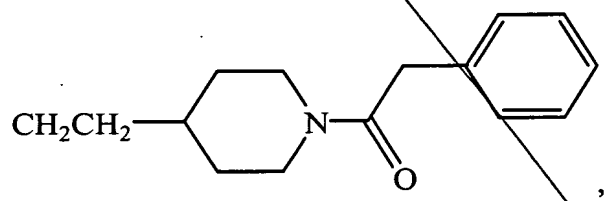
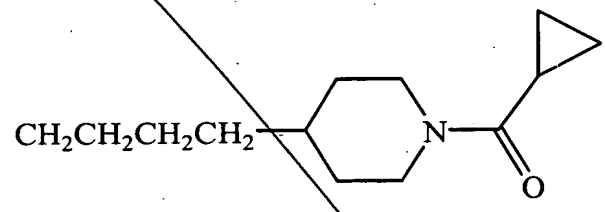
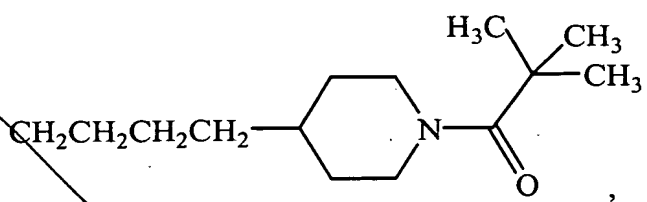
of
cont

C4



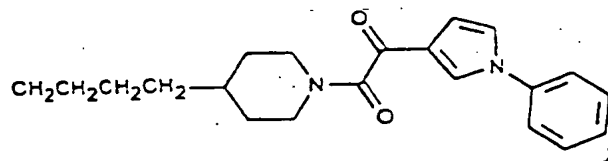
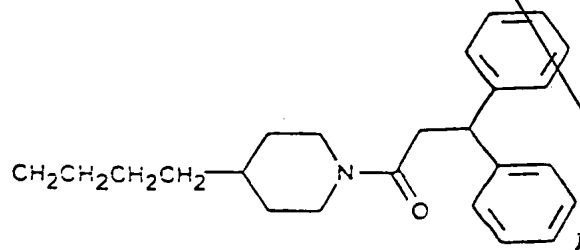
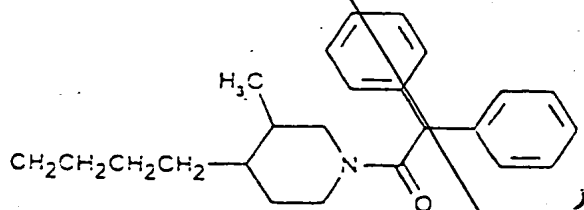
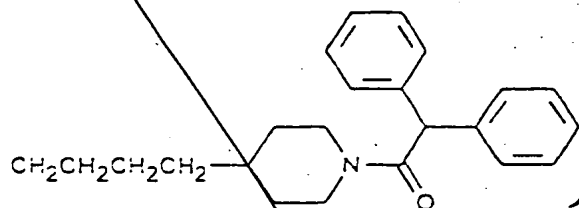
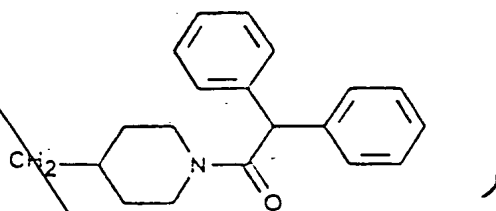
D4
cont

C4



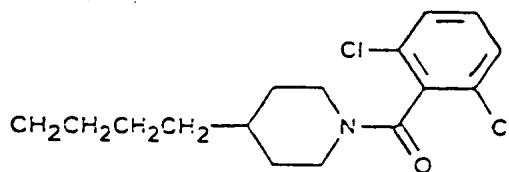
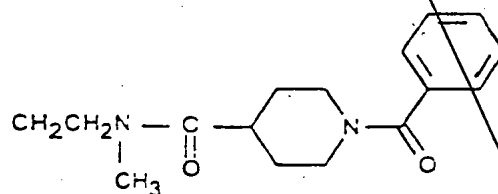
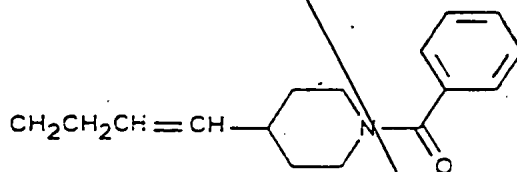
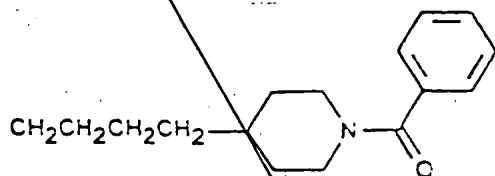
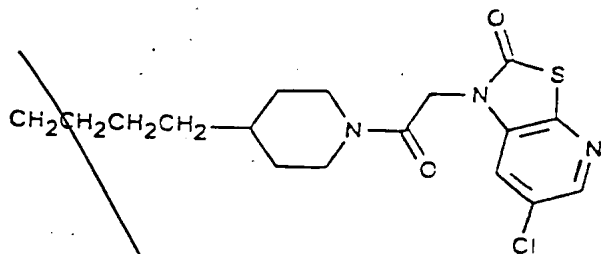
D4
cont

C4



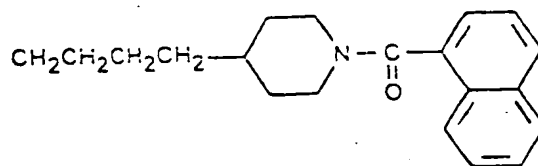
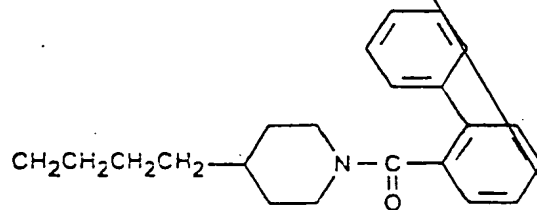
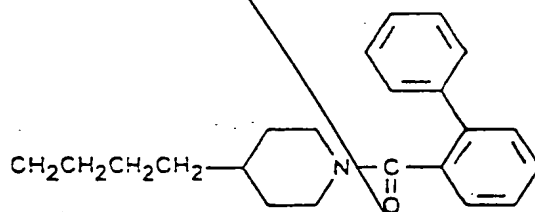
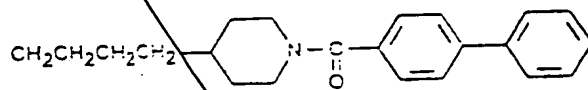
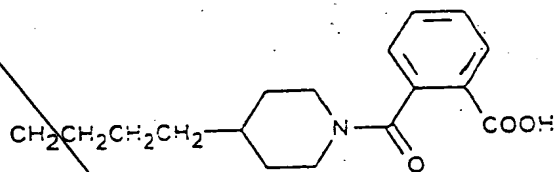
D4
cont

C4



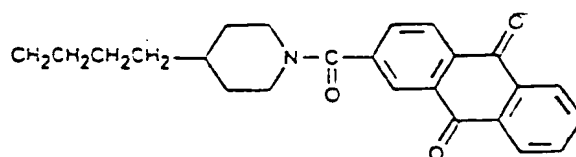
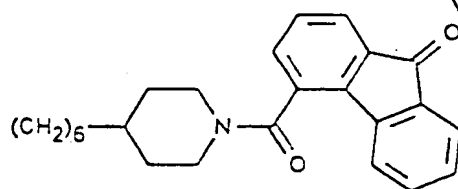
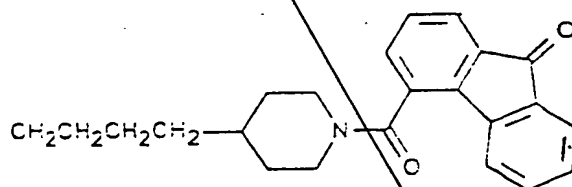
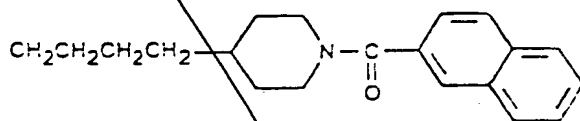
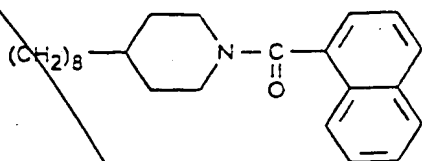
P4
cont

C4



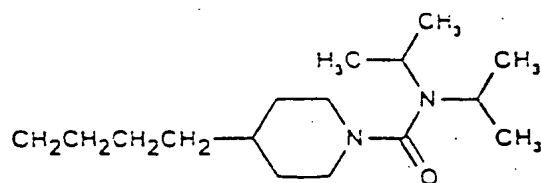
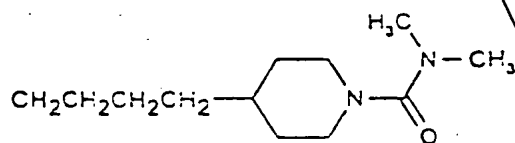
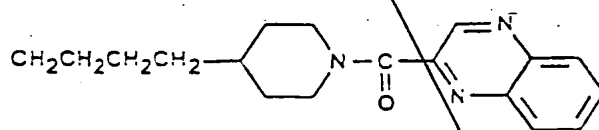
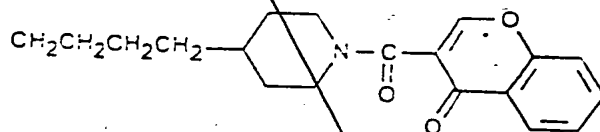
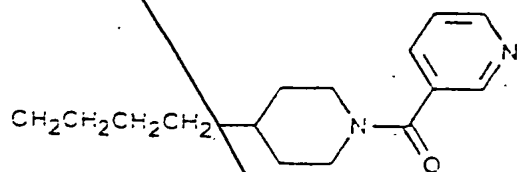
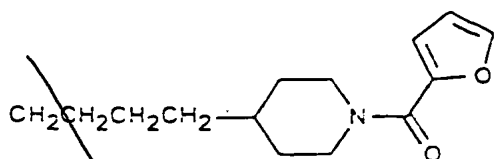
94
cont

C4



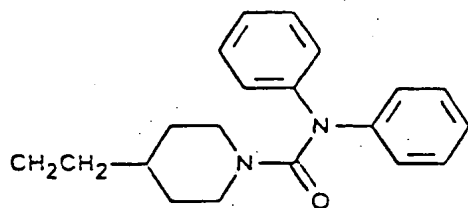
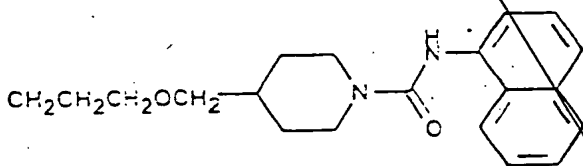
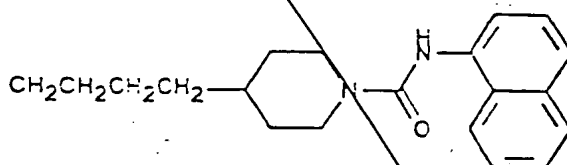
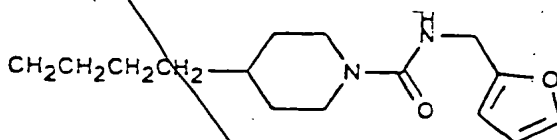
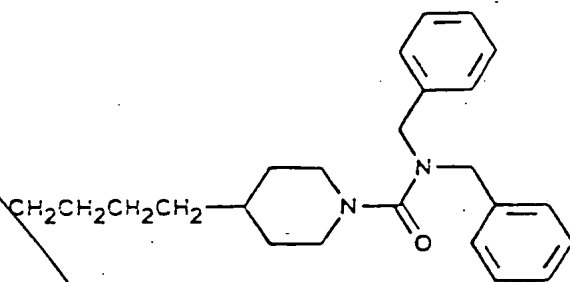
P4
cont

C4



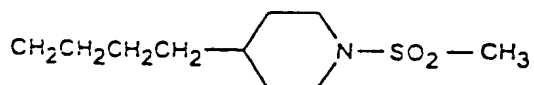
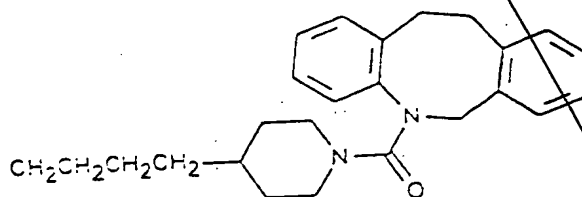
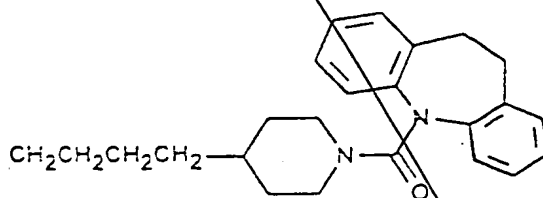
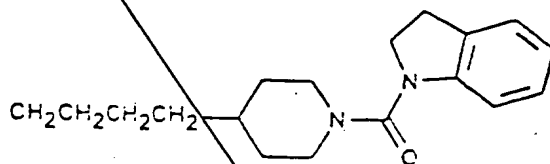
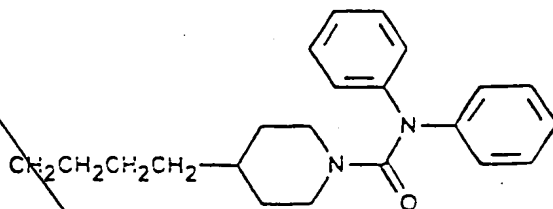
D4
cont

C4



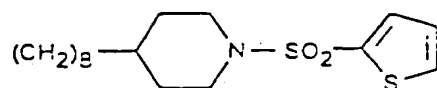
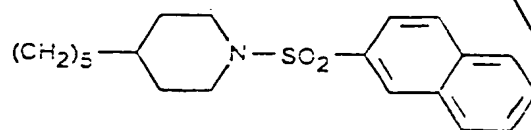
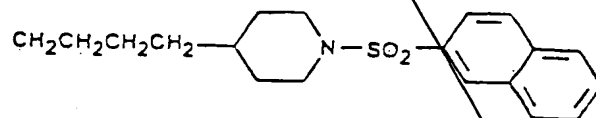
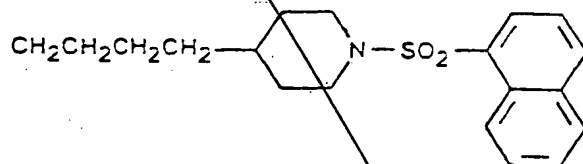
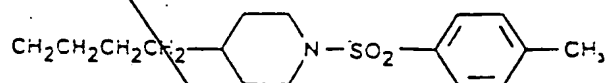
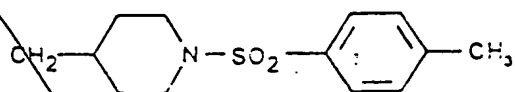
94
cont

C4



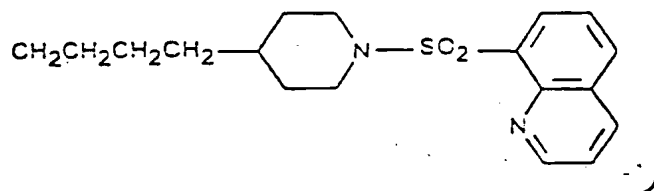
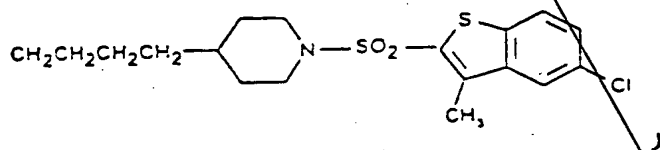
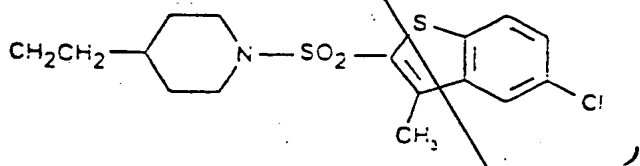
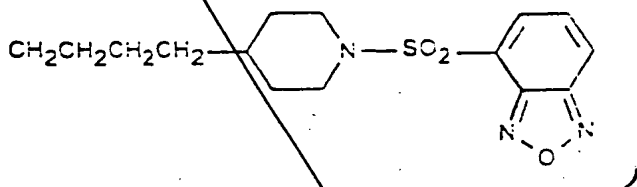
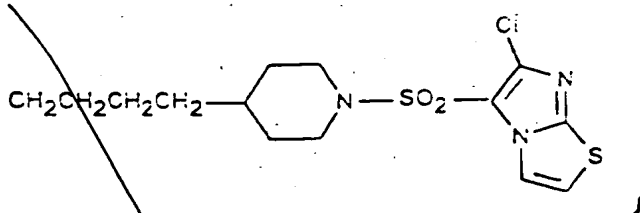
94
cont

C4



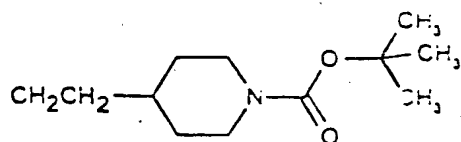
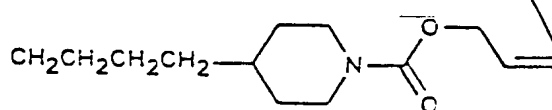
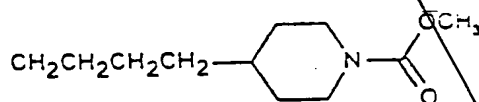
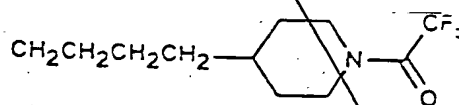
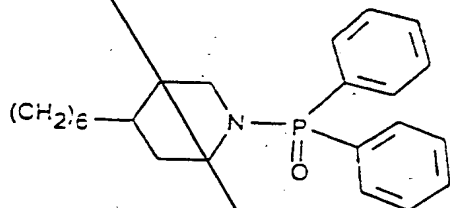
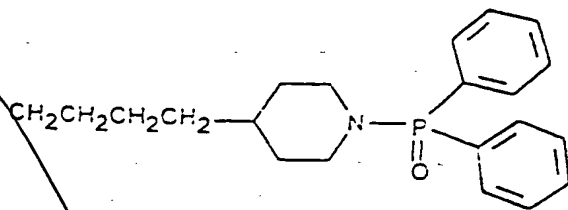
04
cont

C4



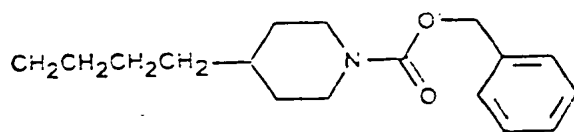
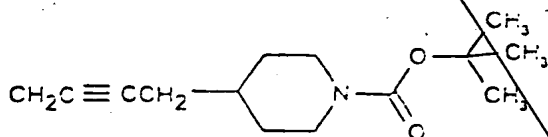
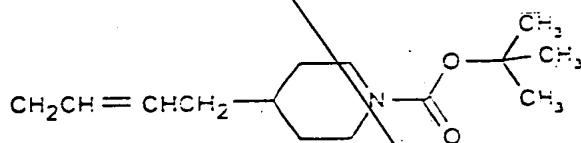
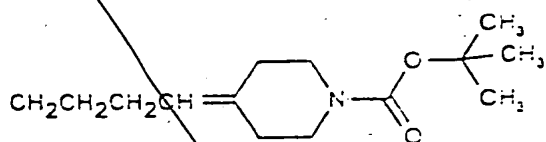
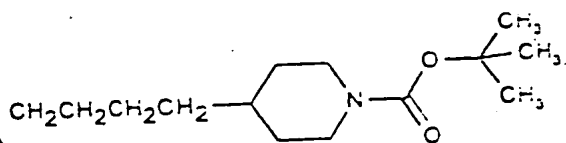
D4
cont

C4



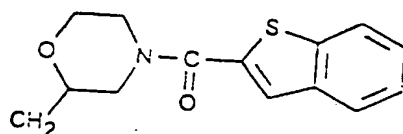
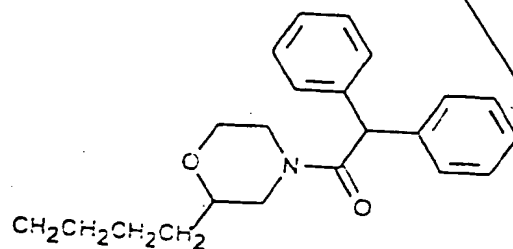
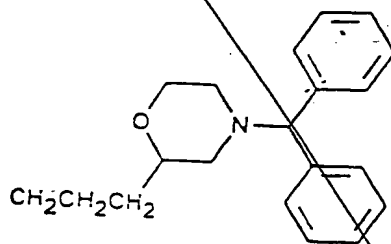
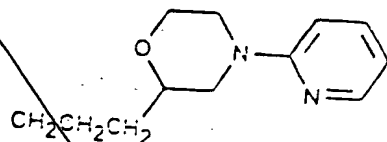
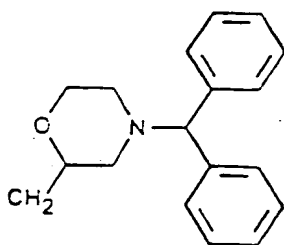
D4
cont

C4



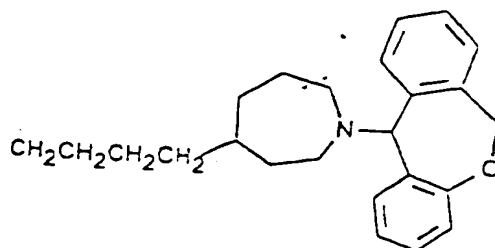
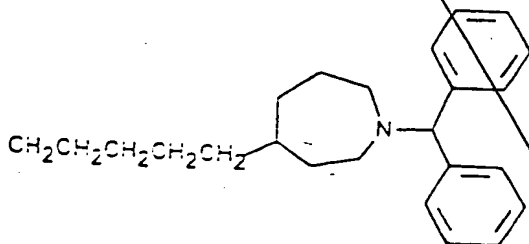
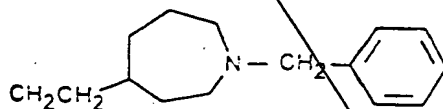
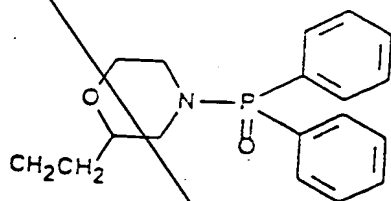
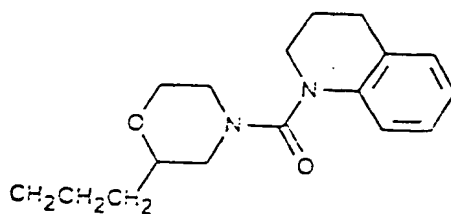
g4
cont

C4



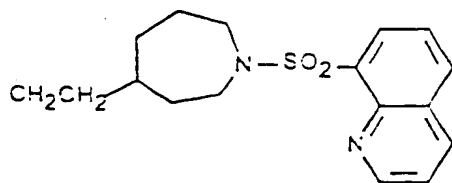
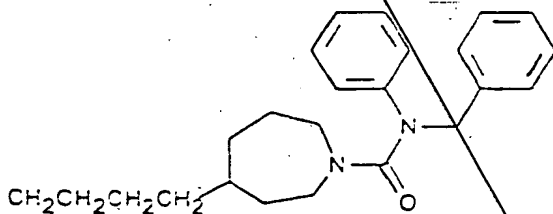
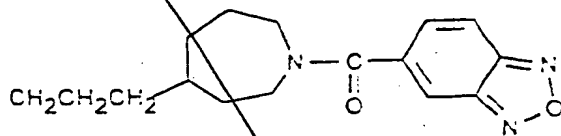
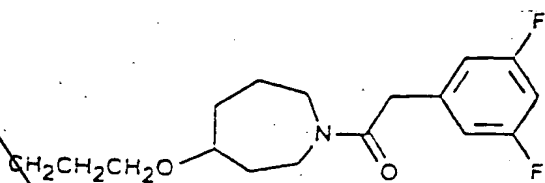
94
cont

C4



94
cont

C4



Q4
cont

C4

